**Figure 1**

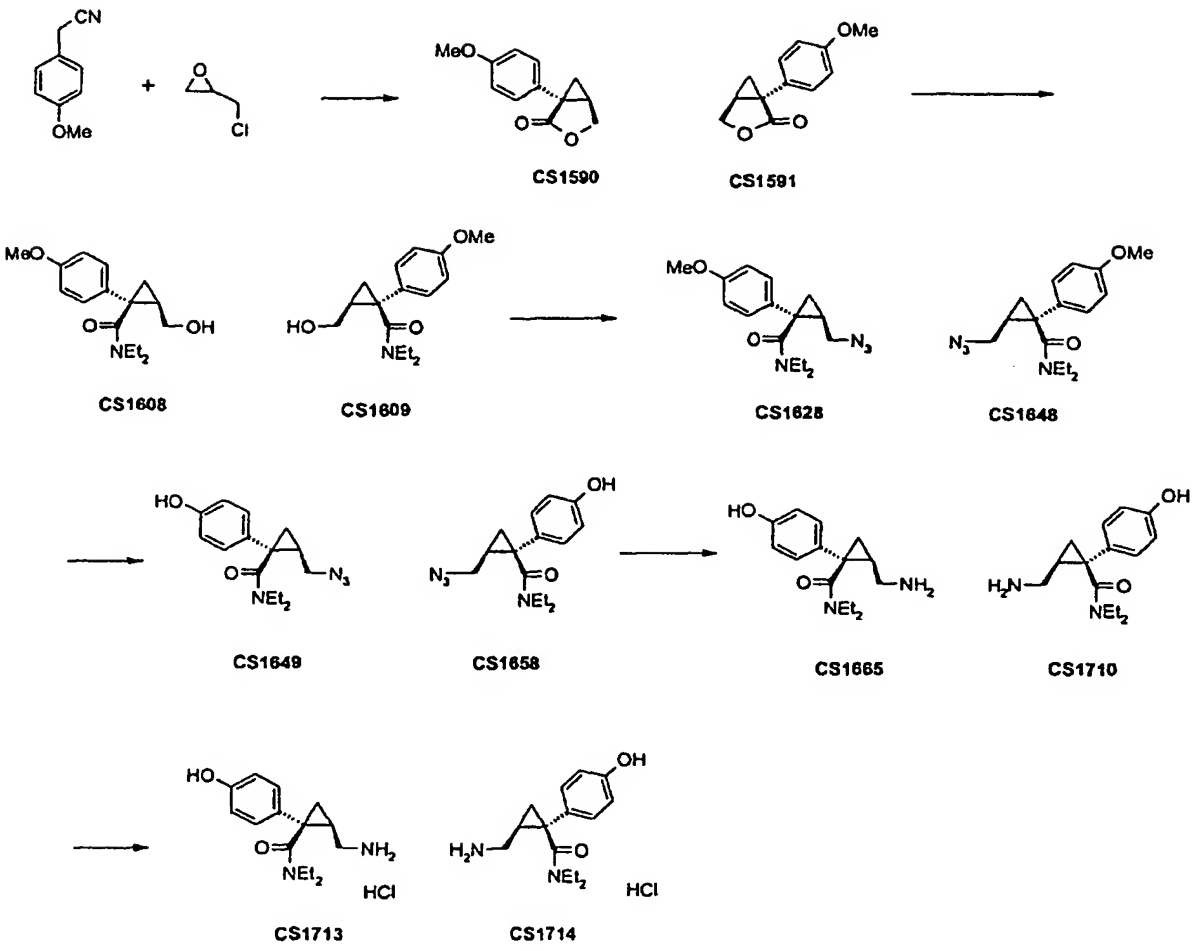

CN
OMe
Cl
MeO
OMe
CS1590
CS1591
MeO
OH
NEt2
CS1608
HO
OMe
NEt2
CS1609
MeO
N3
NEt2
CS1628
OMe
N3
NEt2
CS1648
HO
N3
NEt2
CS1649
OH
N3
NEt2
CS1658
HO
NH2
NEt2
CS1665
OH
H2N
NEt2
CS1710
HO
NH2
NEt2
HCl
CS1713
OH
H2N
NEt2
HCl
CS1714

**Figure 2**

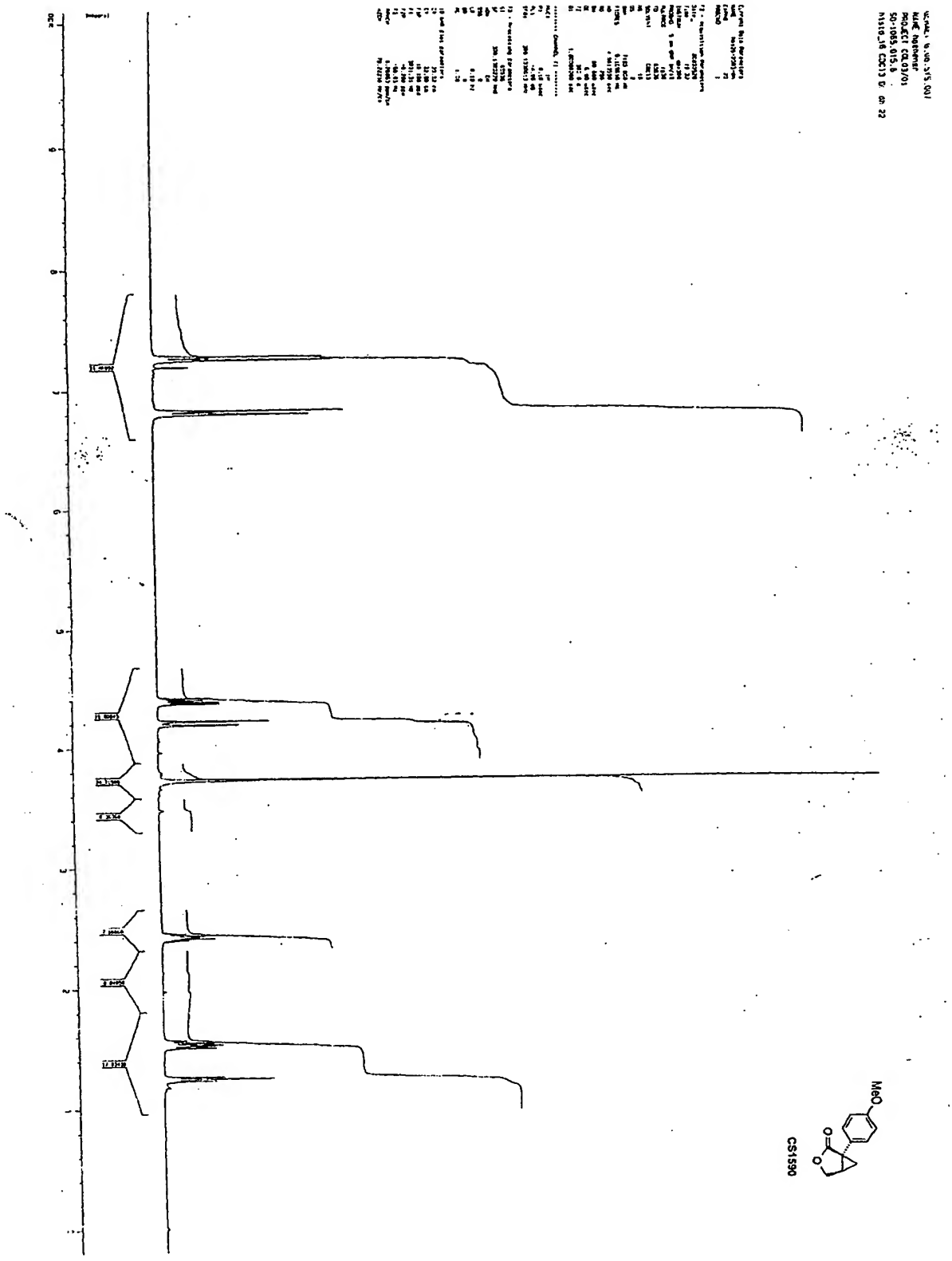


**Figure 3**

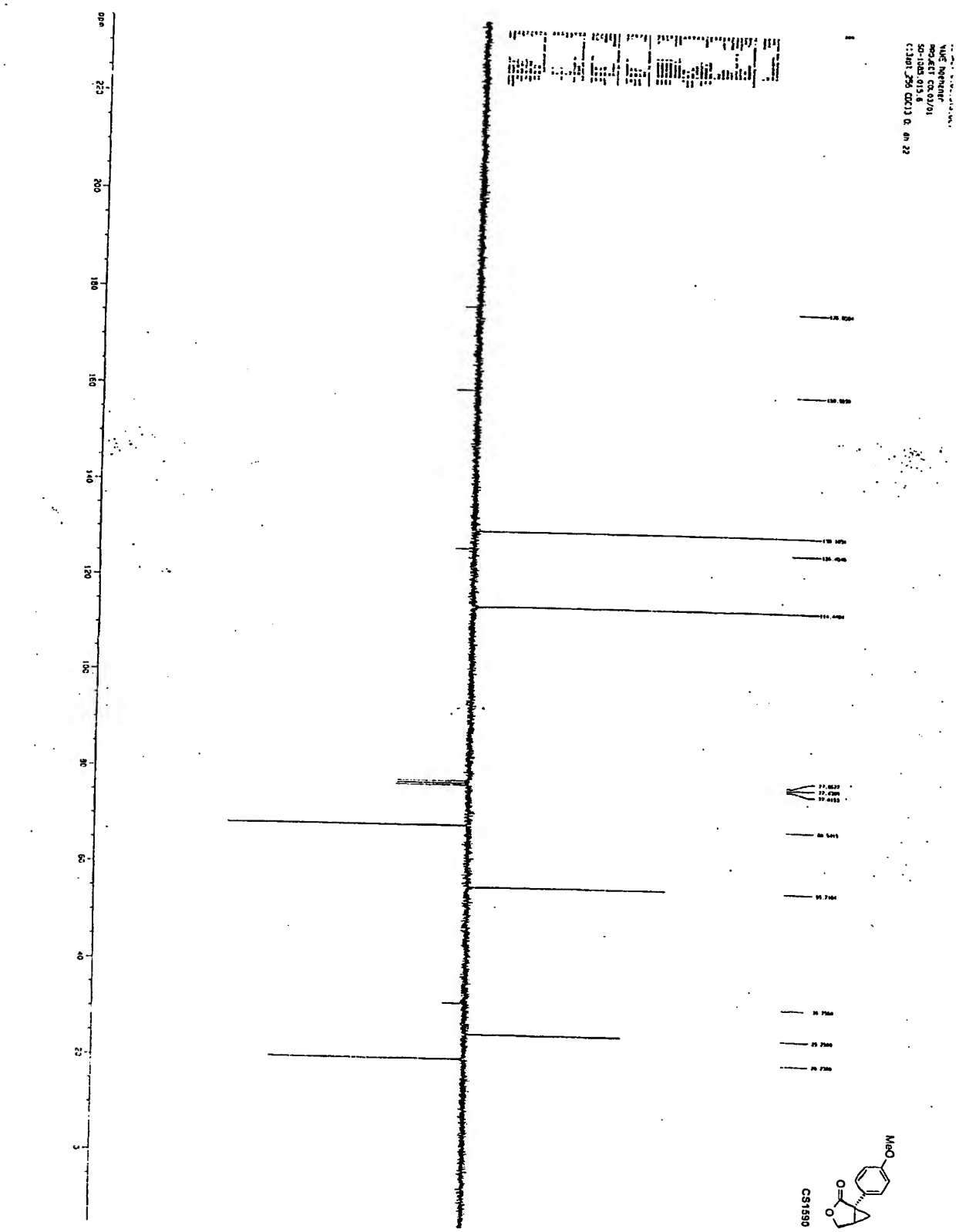


**Figure 4**

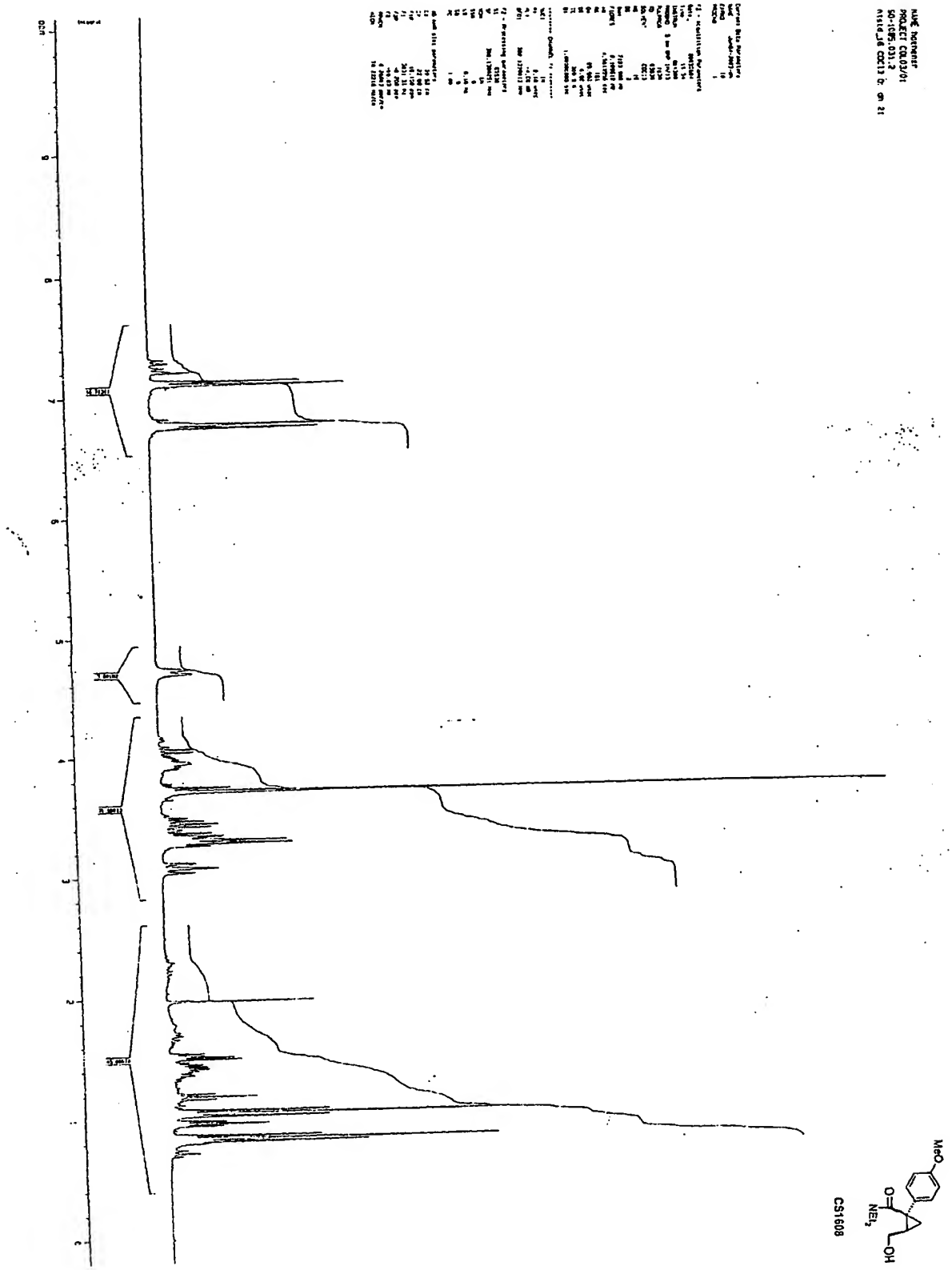


**Figure 5**

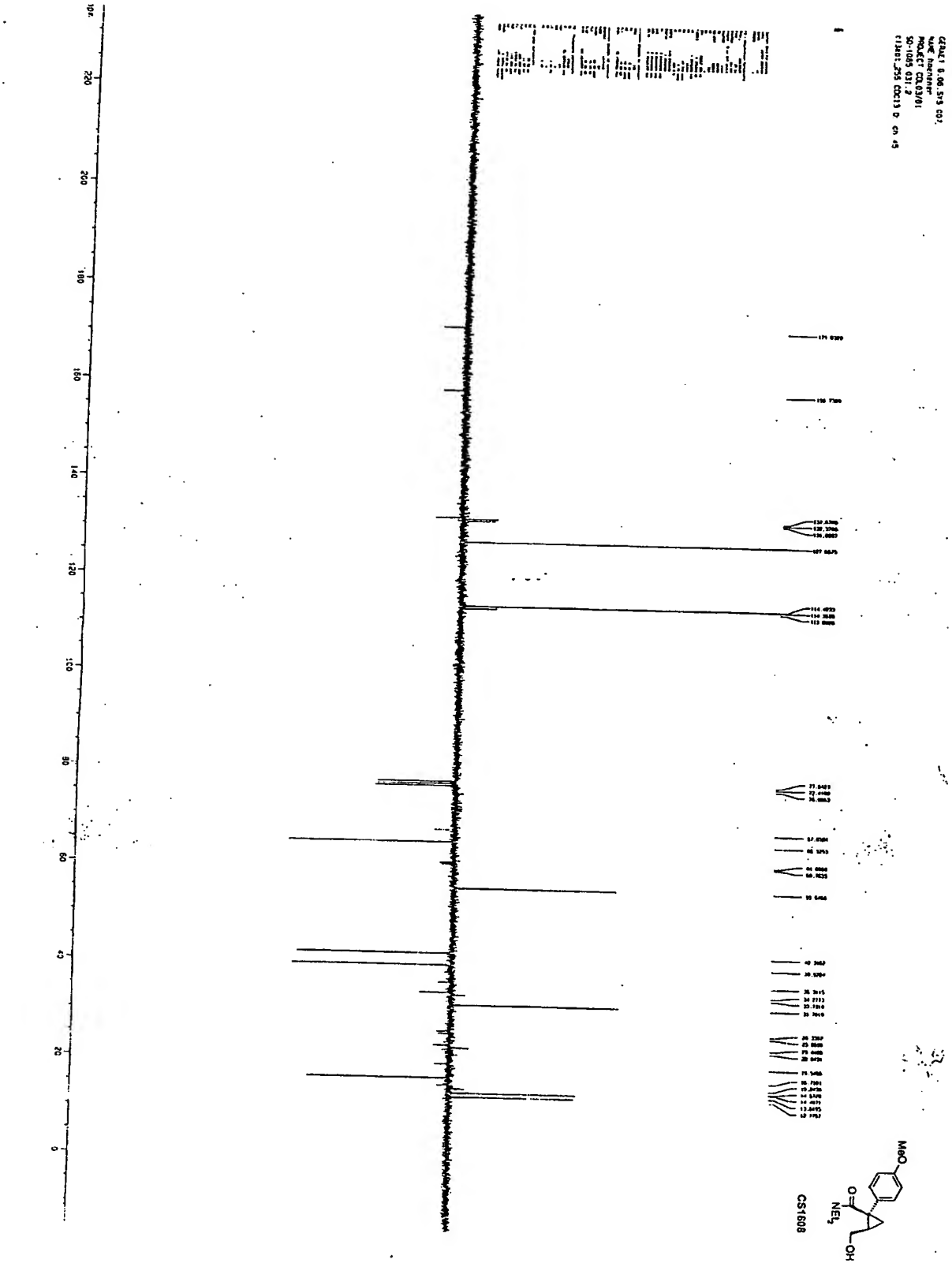


**Figure 6**

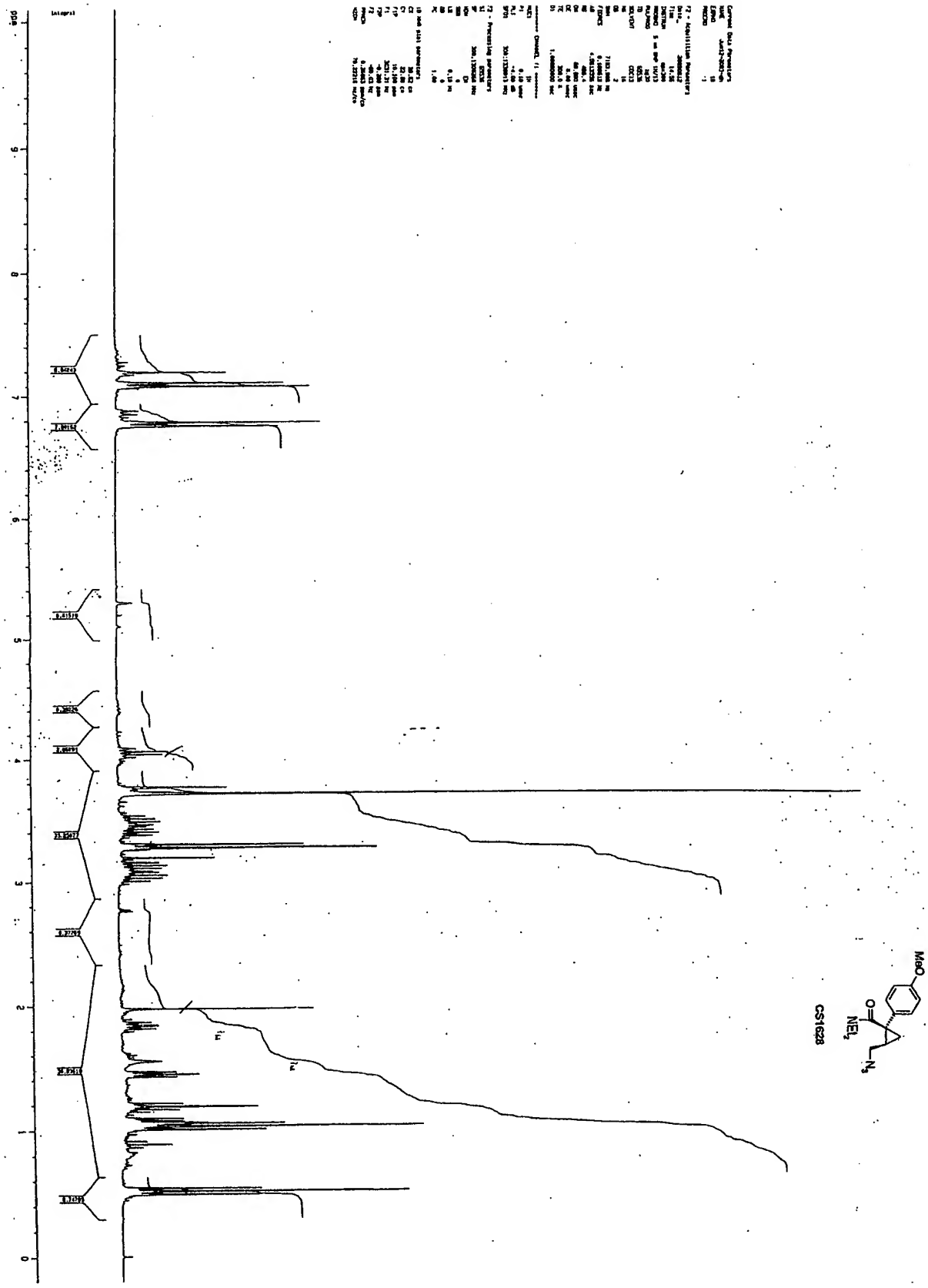


**Figure 7**

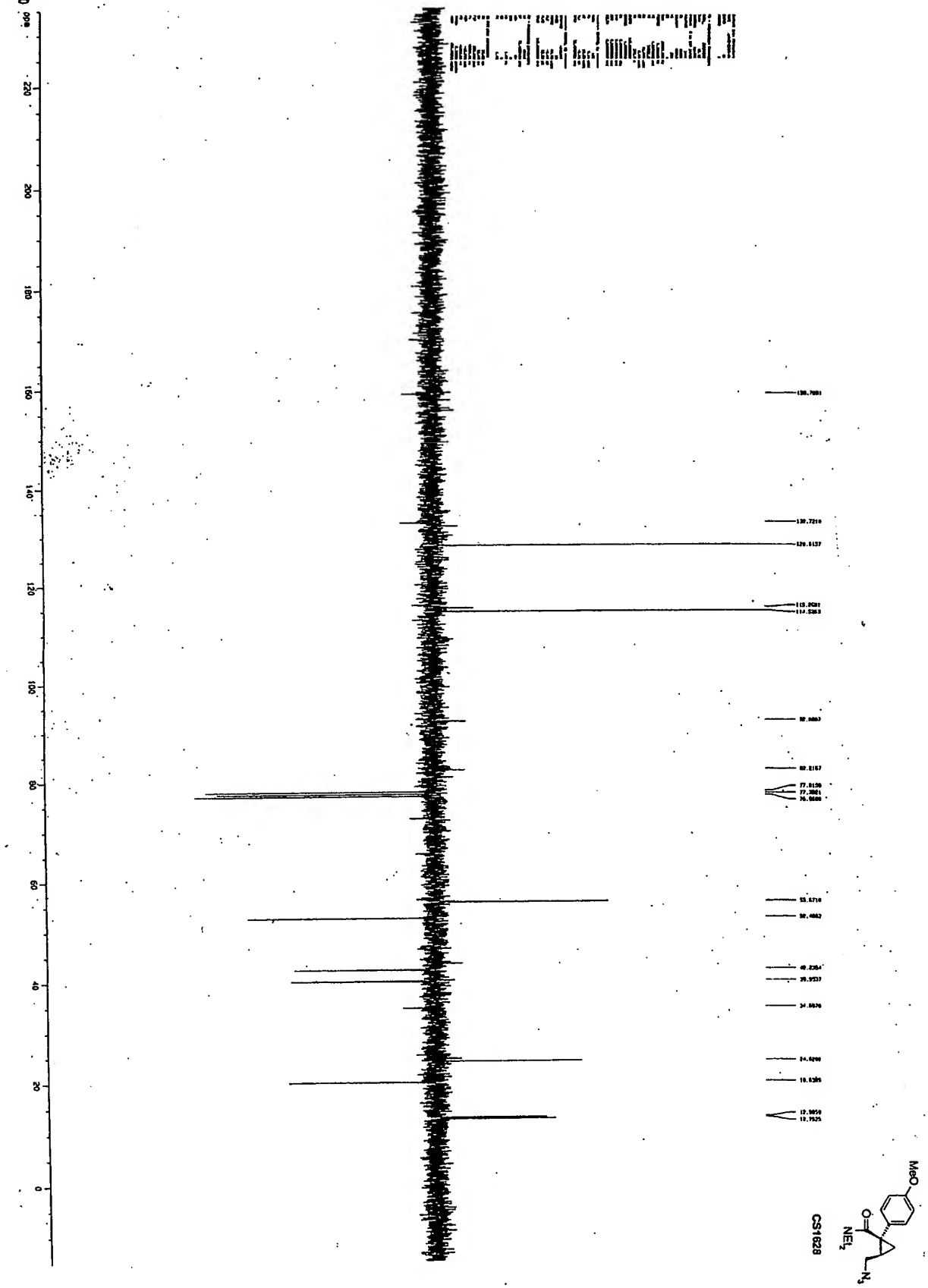


**Figure 8**

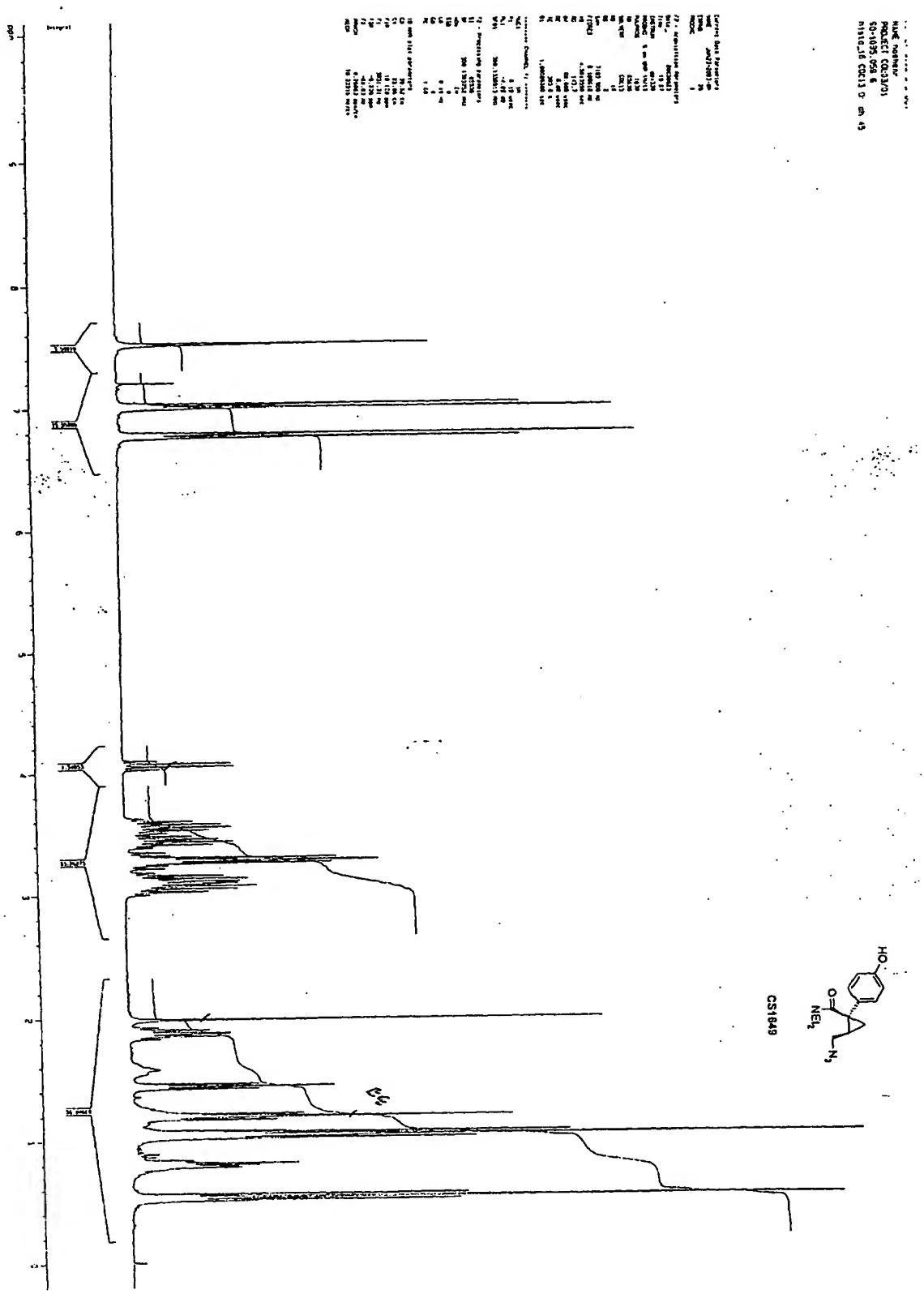


**Figure 9**

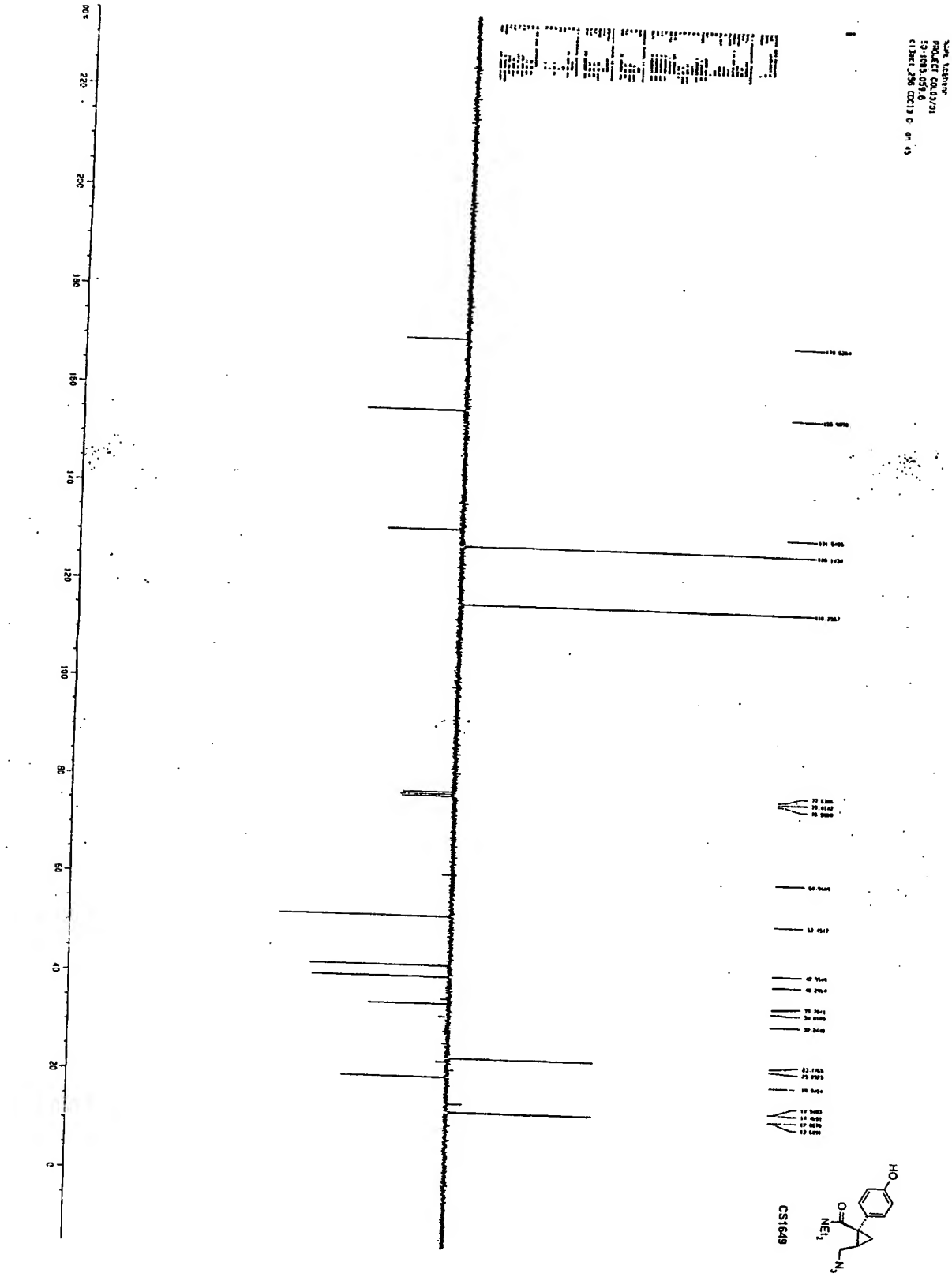
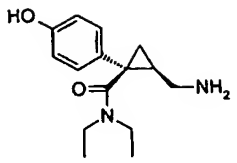


**Figure 10**




**CS1665/2**

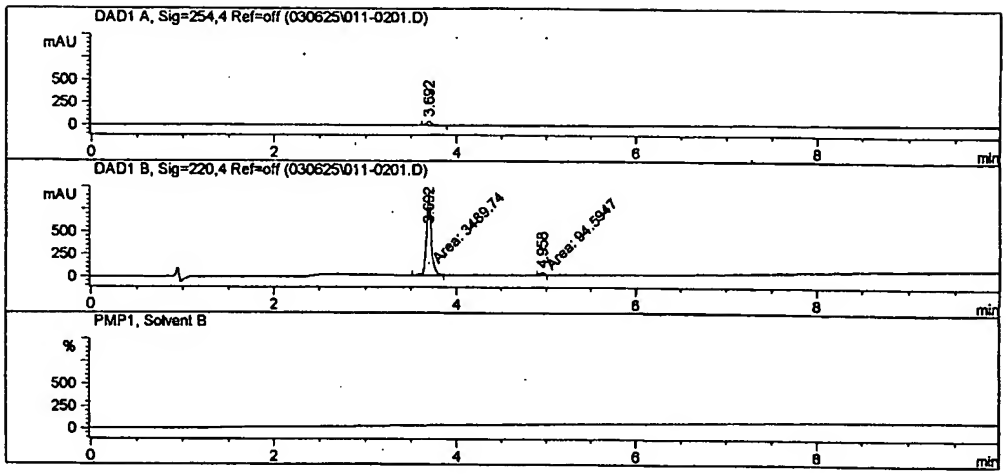


**Figure 11**

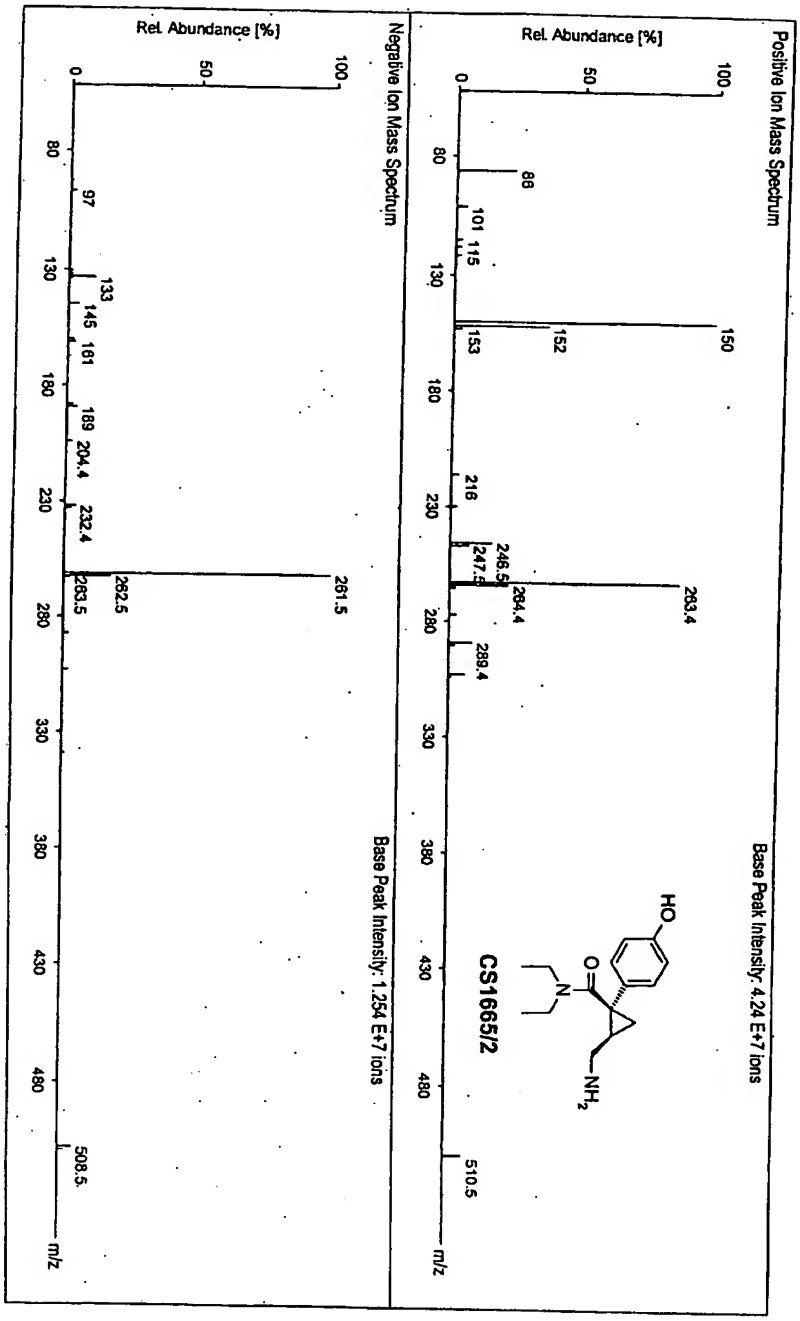

Positive Ion Mass Spectrum
Rel. Abundance [%]
Base Peak Intensity: 4.24 E+7 ions
CS1665/2
m/z
Negative Ion Mass Spectrum
Rel. Abundance [%]
Base Peak Intensity: 1.254 E+7 ions
m/z

**Figure 12**

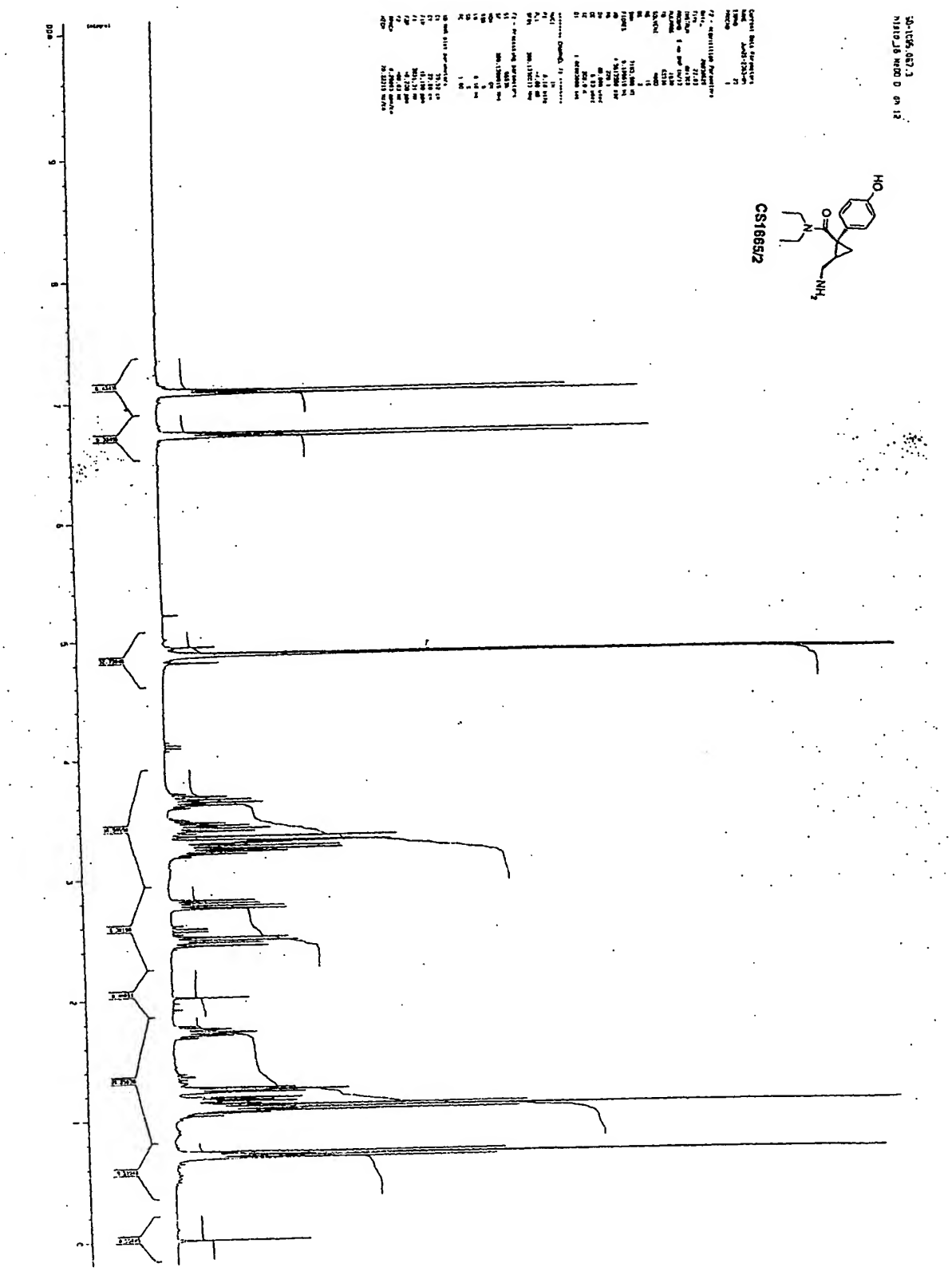


**Figure 13**

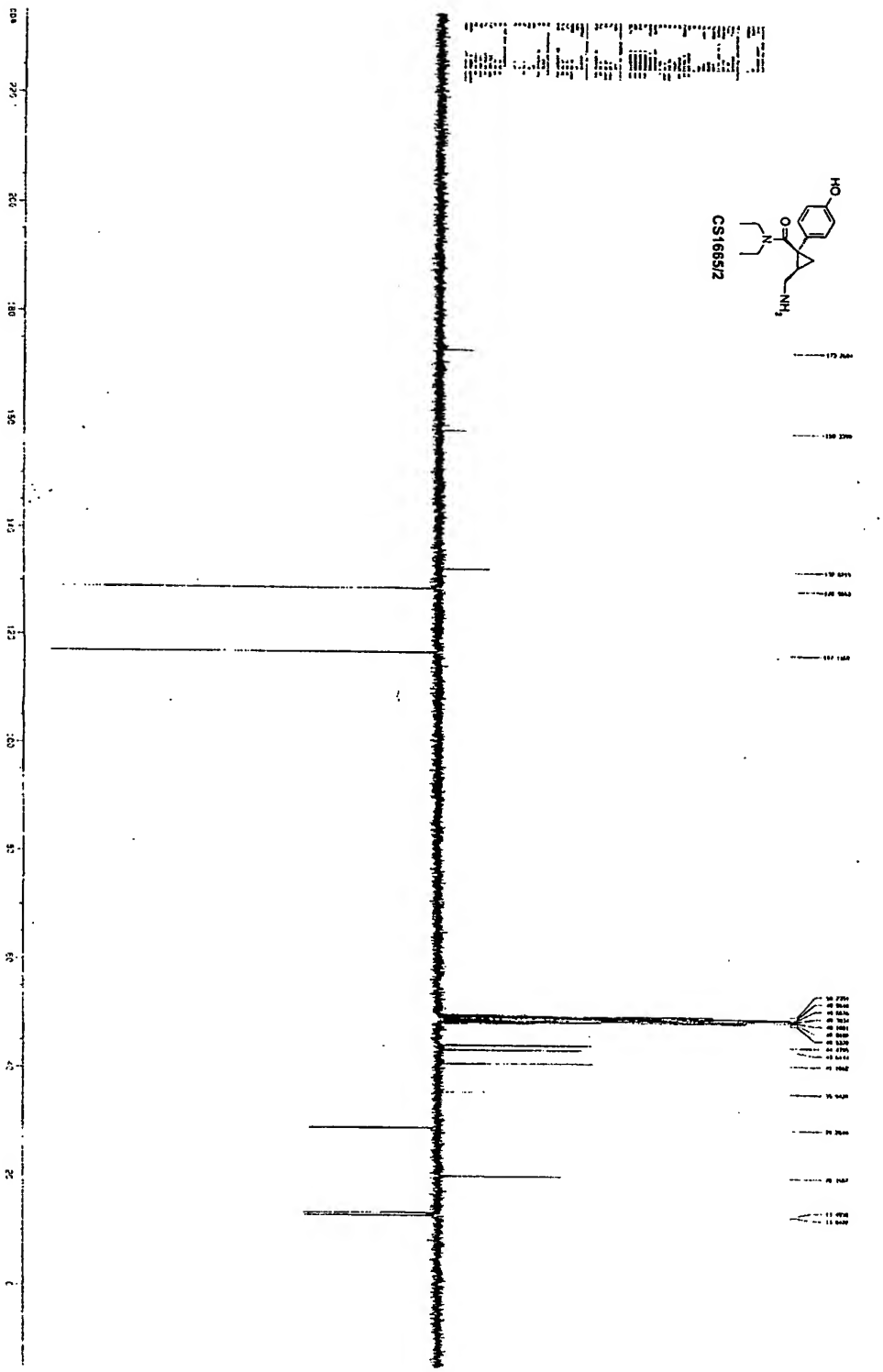
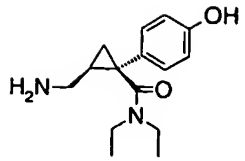


**Figure 14**




**CS1710/1**

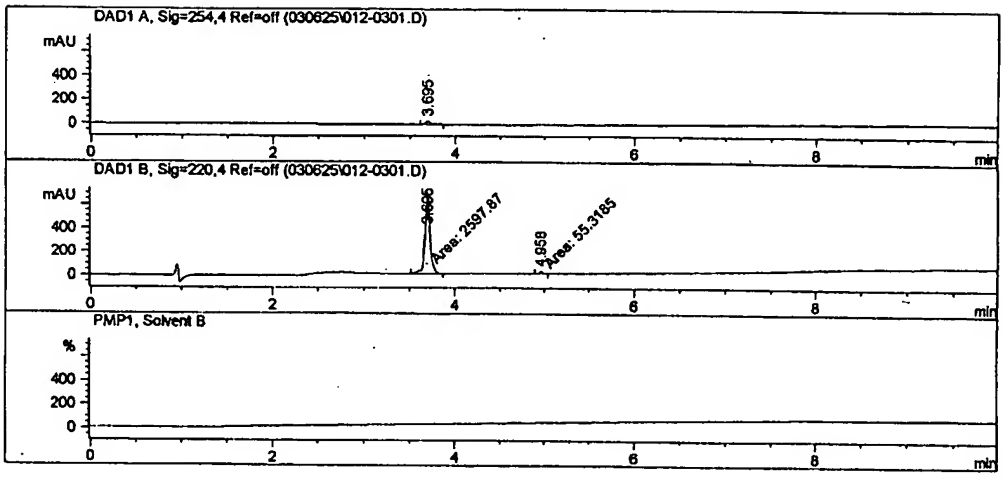


**Figure 15**

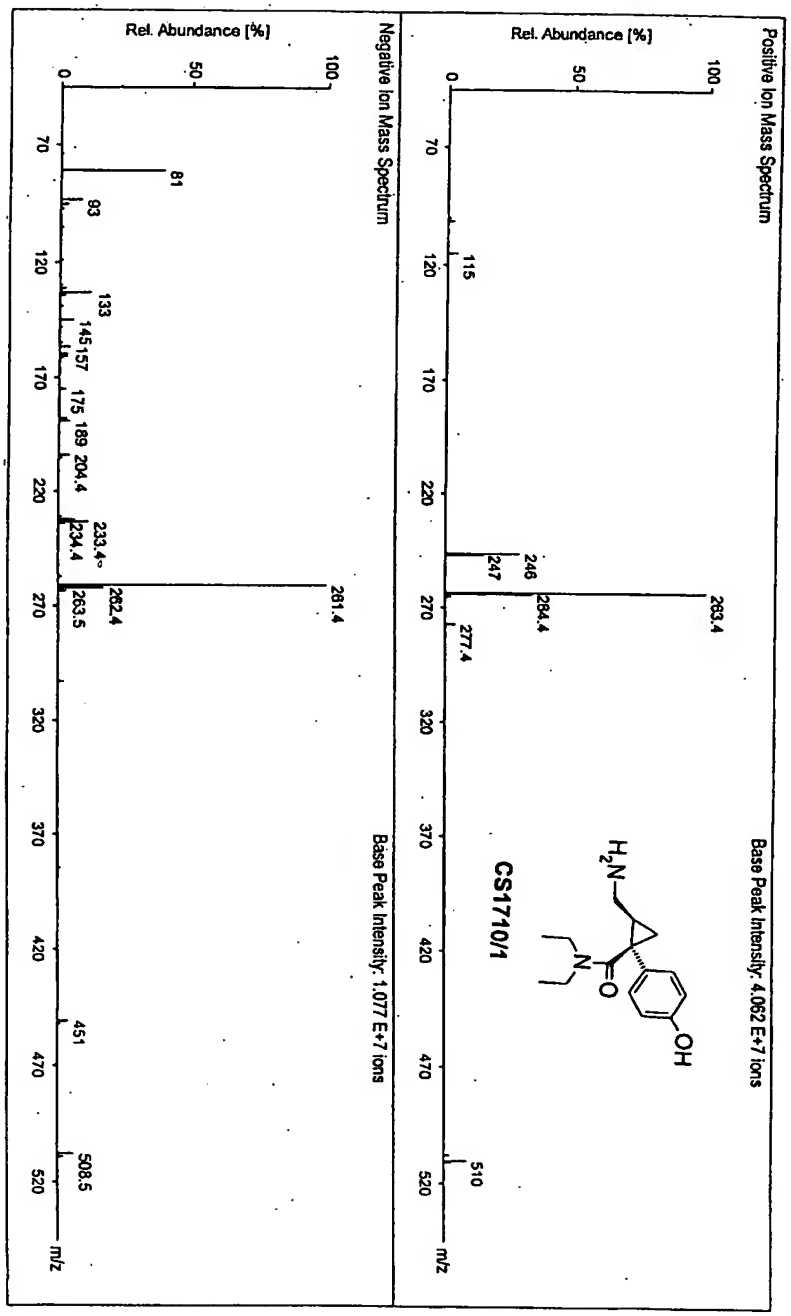

Positive Ion Mass Spectrum
Rel. Abundance [%]
Base Peak Intensity: 4.062 E+7 ions
263.4
284.4
246
247
277.4
115
CS1710/1
Negative Ion Mass Spectrum
Base Peak Intensity: 1.077 E+7 ions
281.4
262.4
263.5
233.4**
234.4
204.4
189
175
157
145
133
93
81
m/z

**Figure 16**

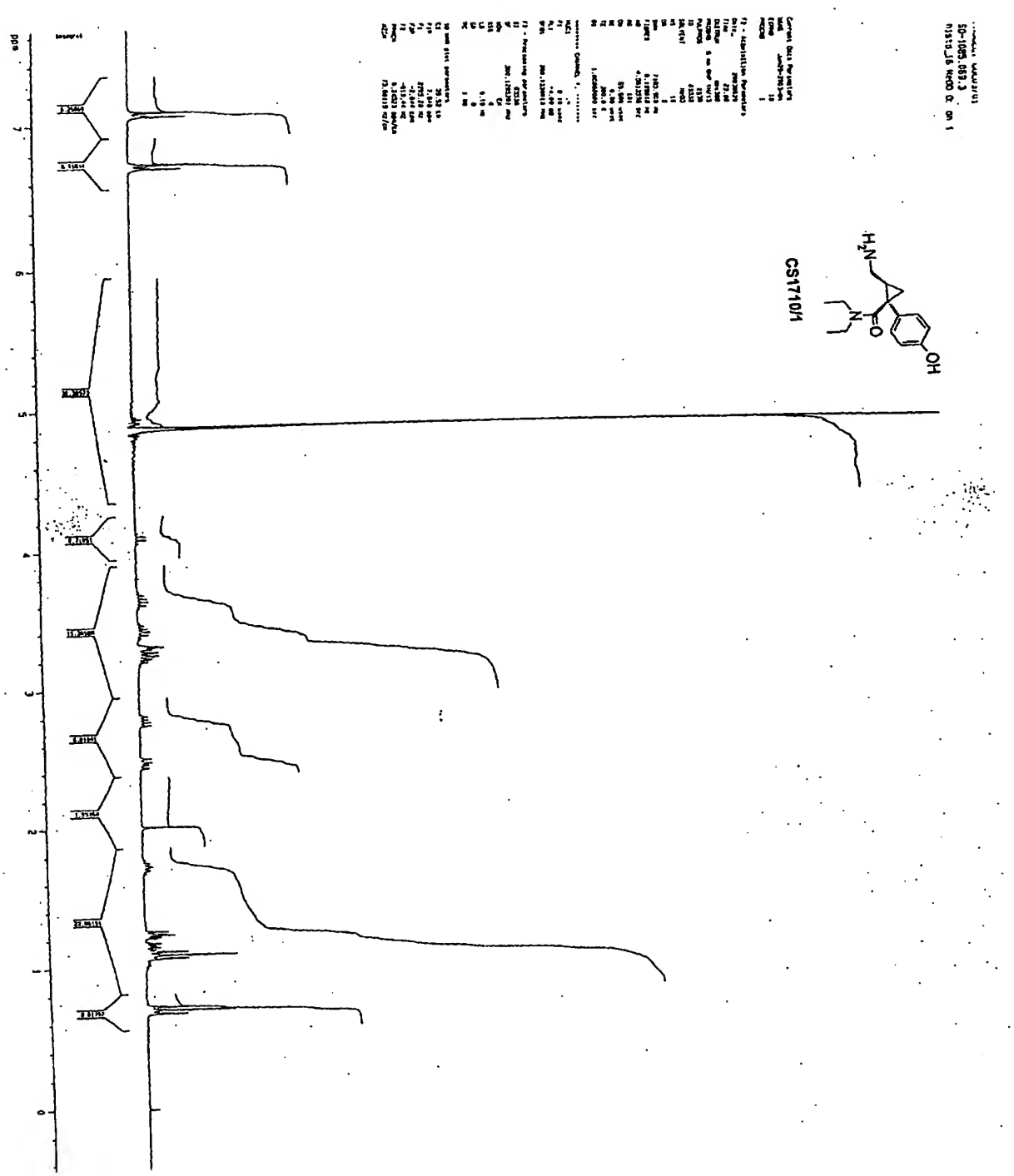


**Figure 17**

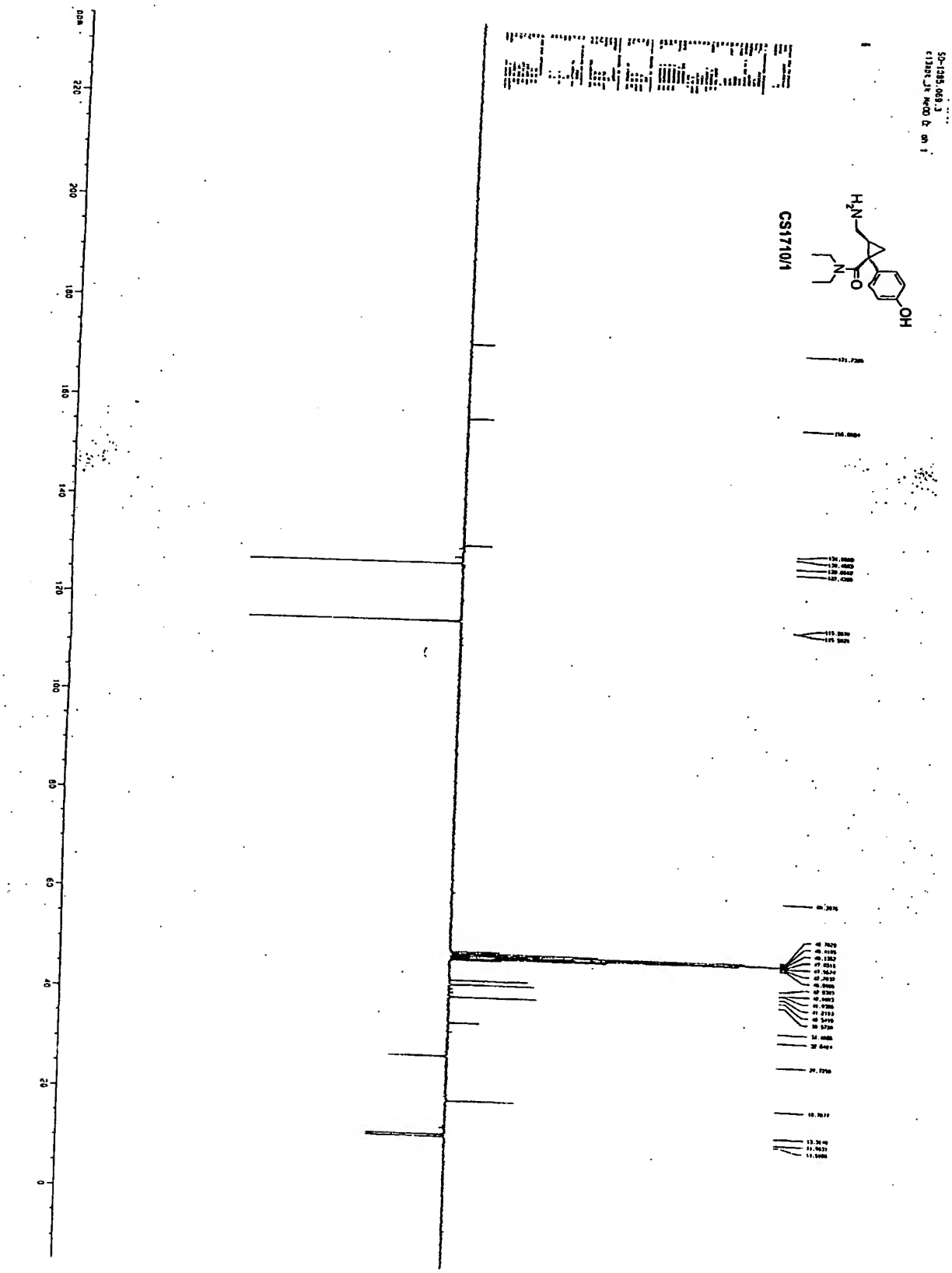


**Figure 18**

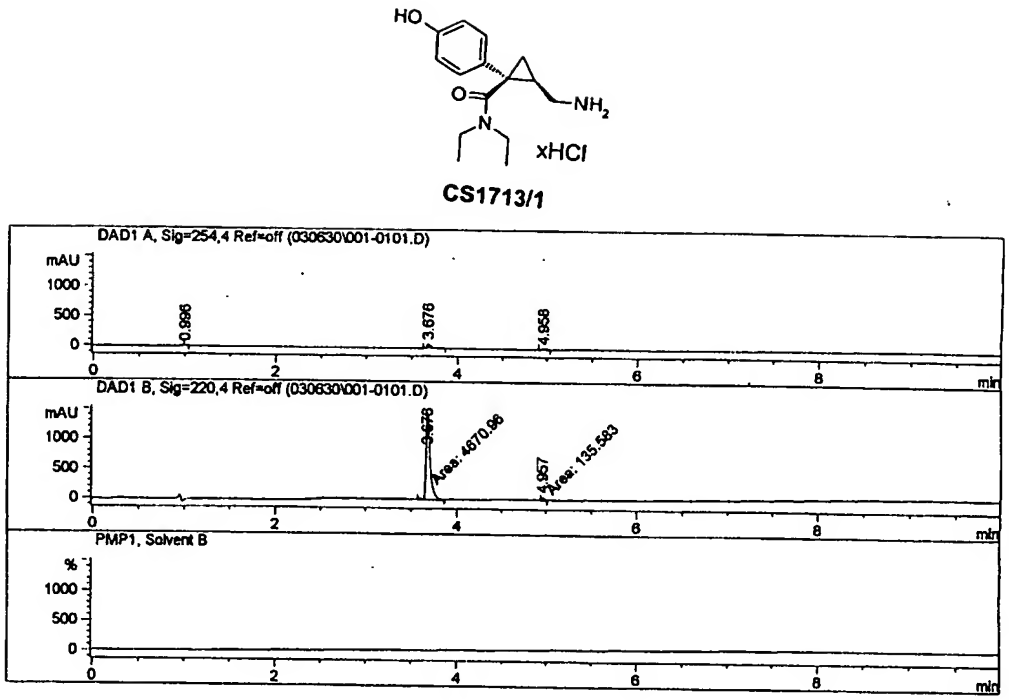

HO
O
N
NH2
xHCl
CS1713/1
DAD1 A, Sig=254,4 Ref=off (030630\001-0101.D)
mAU
1000
500
0
0.996
3.676
4.958
0
2
4
6
8
min
DAD1 B, Sig=220,4 Ref=off (030630\001-0101.D)
mAU
1000
500
0
3.678
Area: 4870.96
4.957
Area: 135.583
0
2
4
6
8
min
PMP1, Solvent B
%
1000
500
0
0
2
4
6
8
min

**Figure 19**

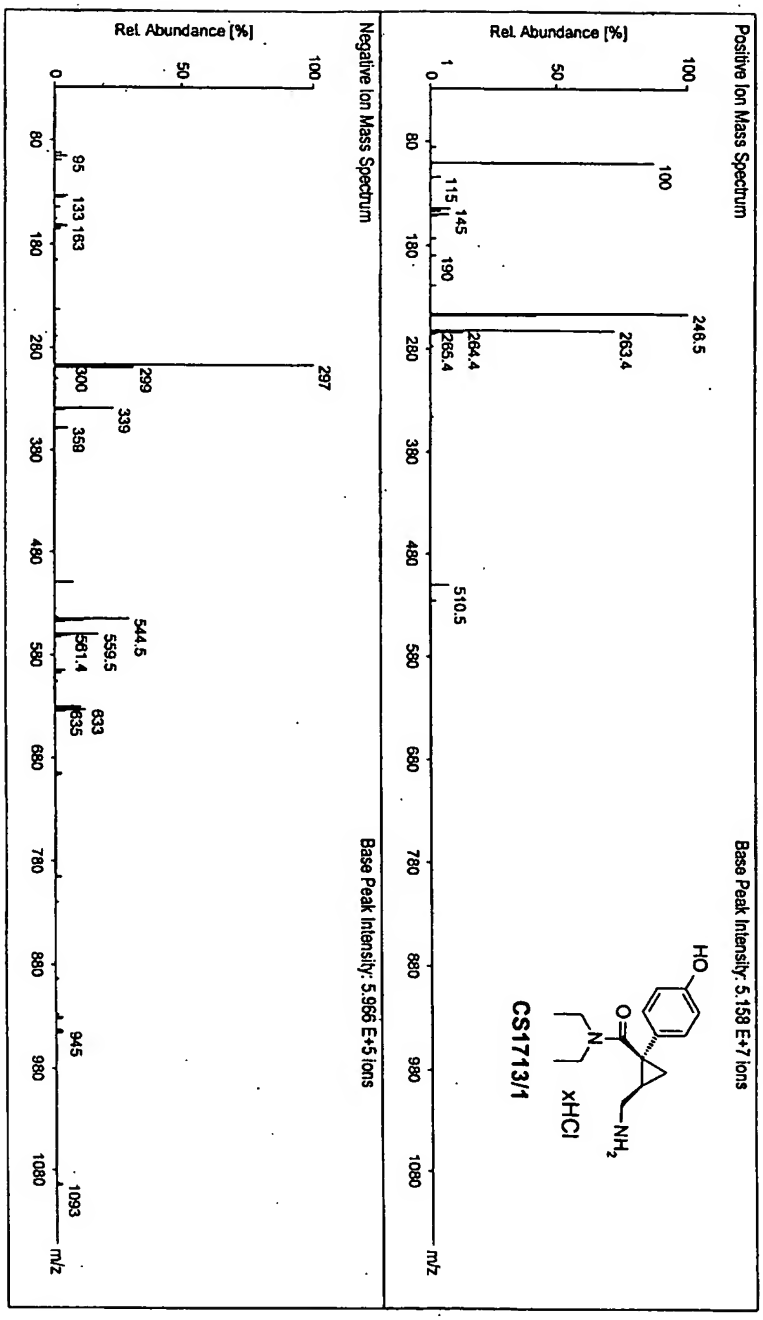

Positive Ion Mass Spectrum
Rel. Abundance [%]
Base Peak Intensity: 5.158 E+7 ions
246.5
263.4
264.4
265.4
510.5
115
145
190
m/z
CS1713/1
xHCl
Negative Ion Mass Spectrum
Base Peak Intensity: 5.966 E+5 ions
297
299
339
544.5
559.5
561.4
633
635
945
1093

**Figure 20**

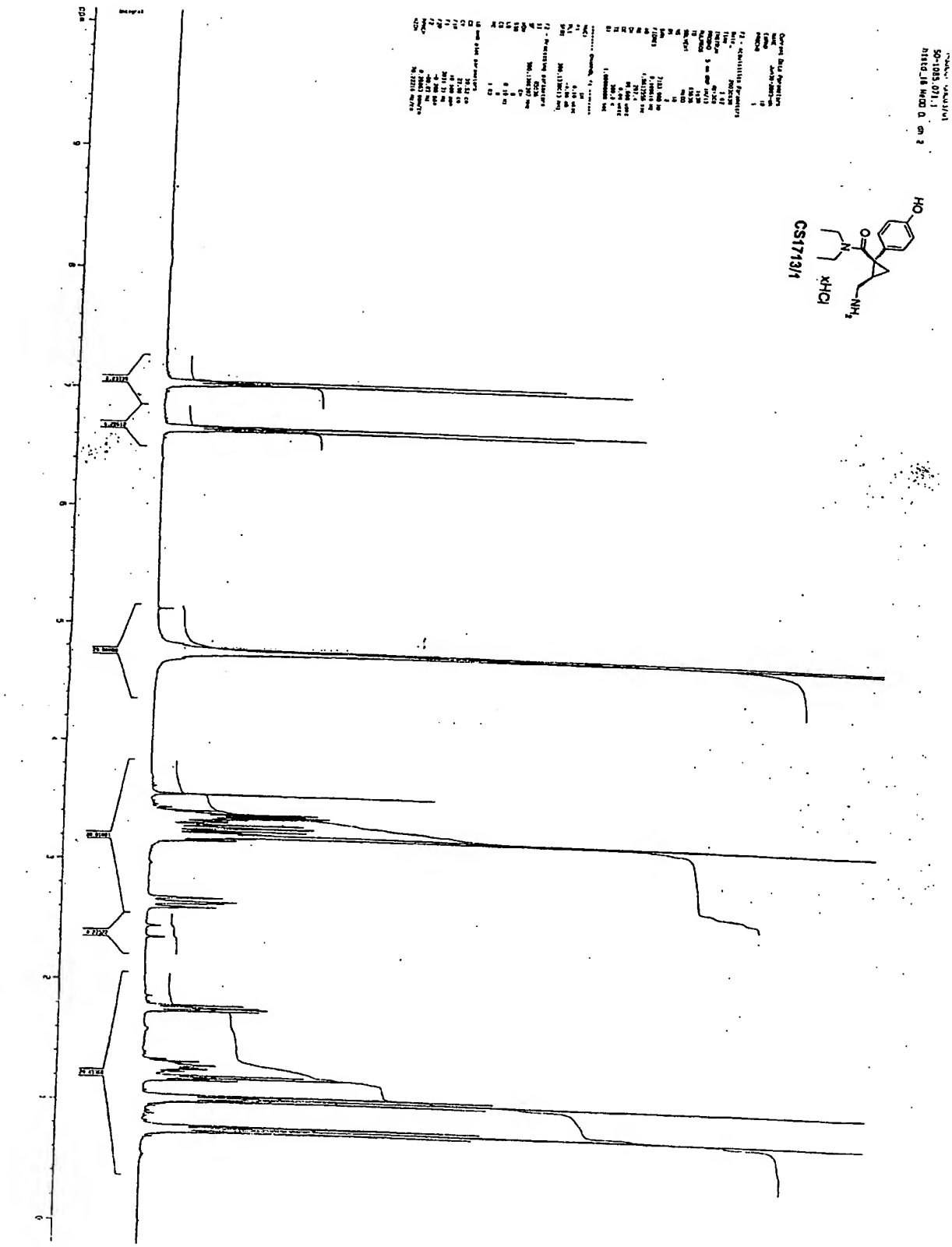


**Figure 21**

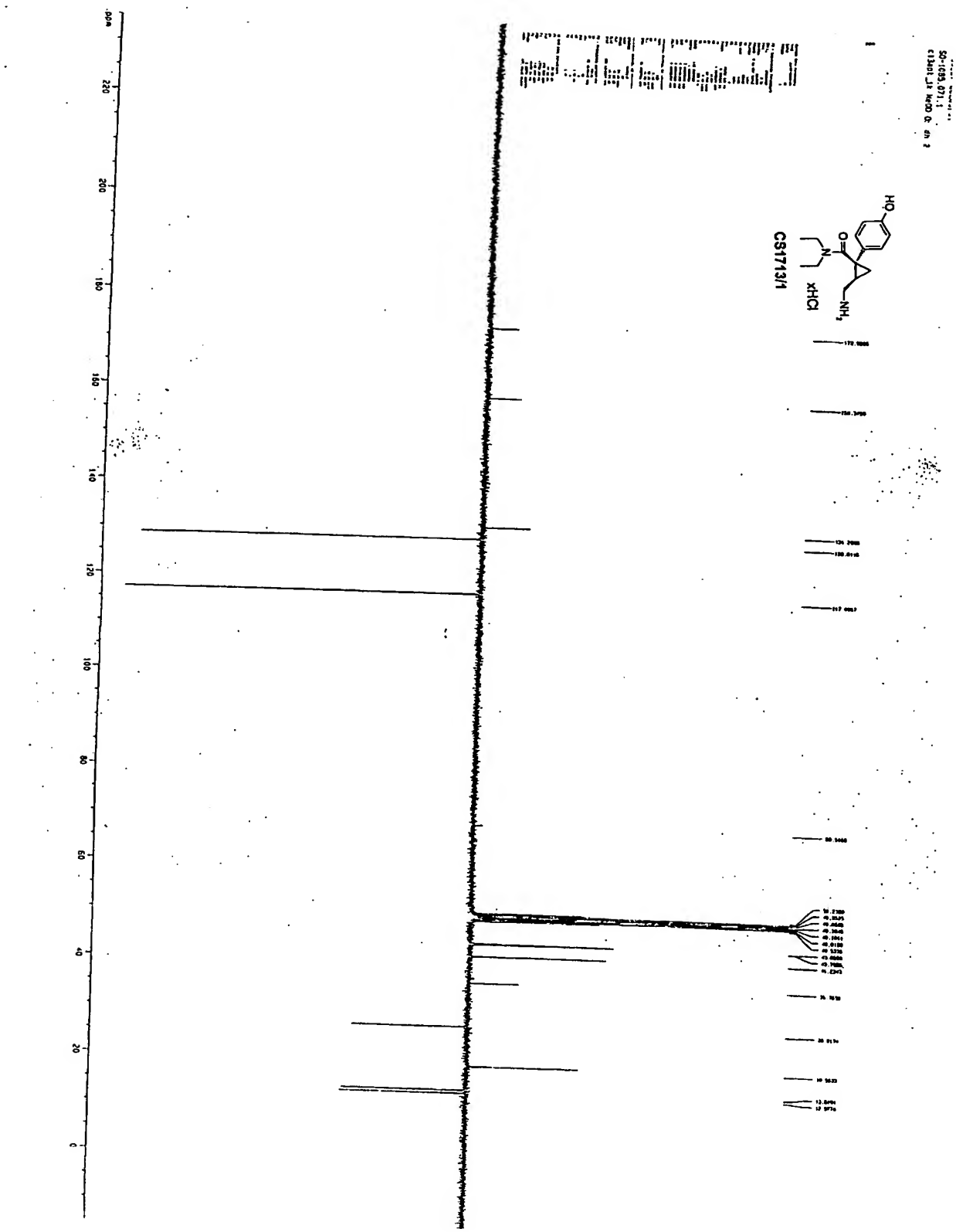
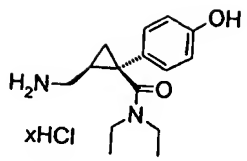


**Figure 22**




**CS1714/1**

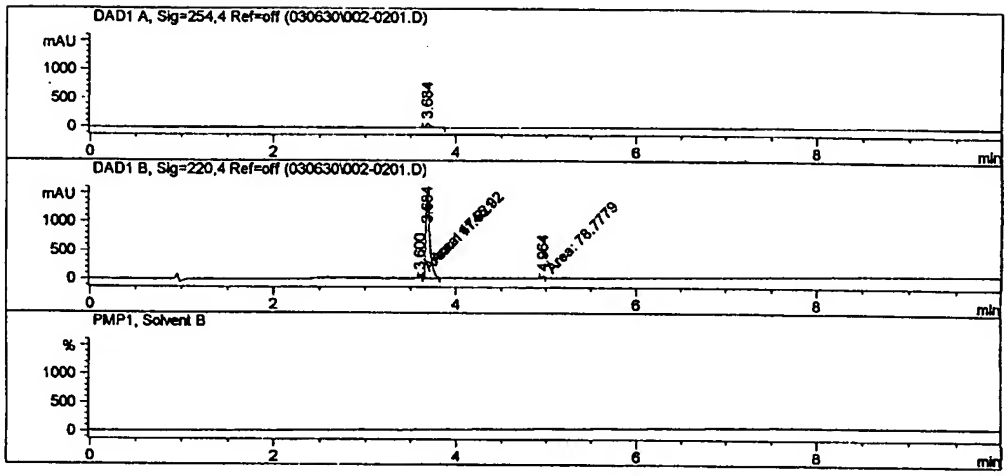


**Figure 23**

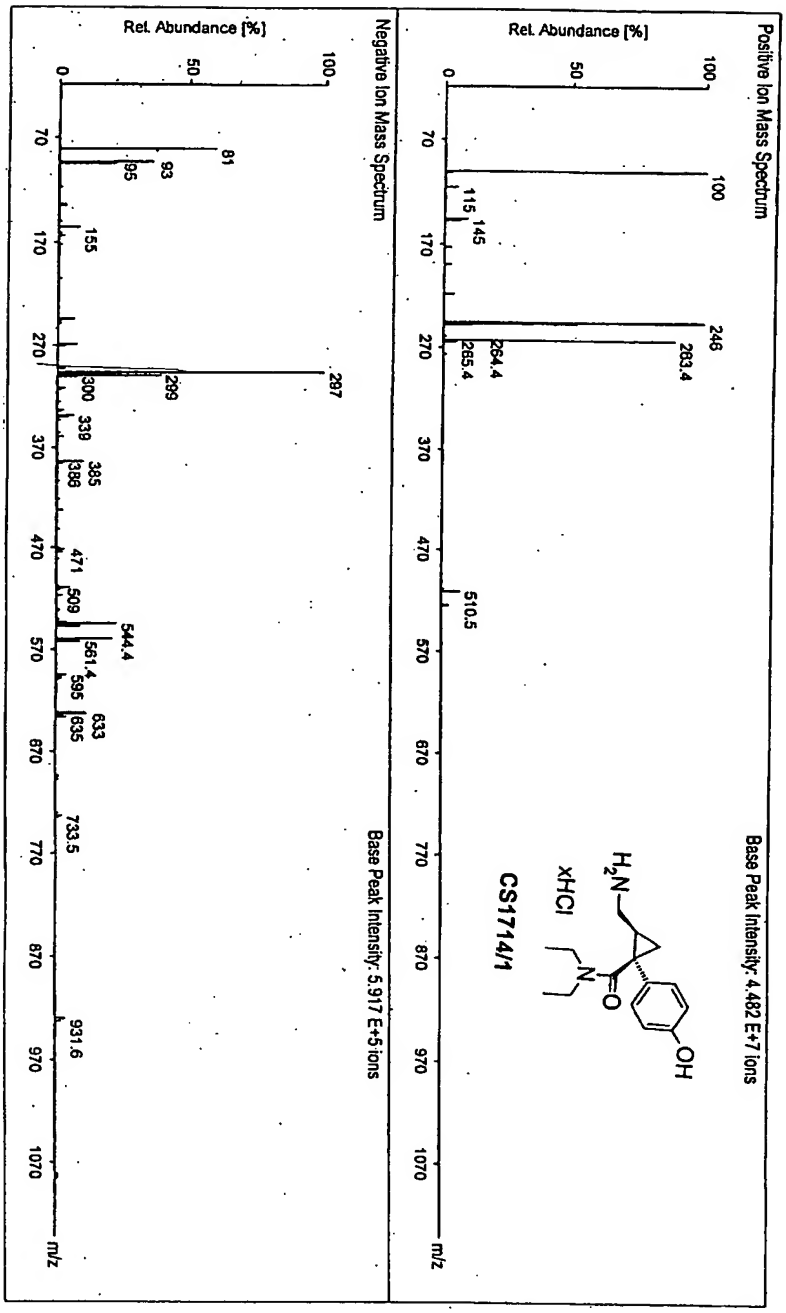

Positive Ion Mass Spectrum
Rel. Abundance [%]
Base Peak Intensity: 4.482 E+7 ions
CS1714/1
xHCl
Negative Ion Mass Spectrum
Base Peak Intensity: 5.917 E+5 ions
m/z

**Figure 24**

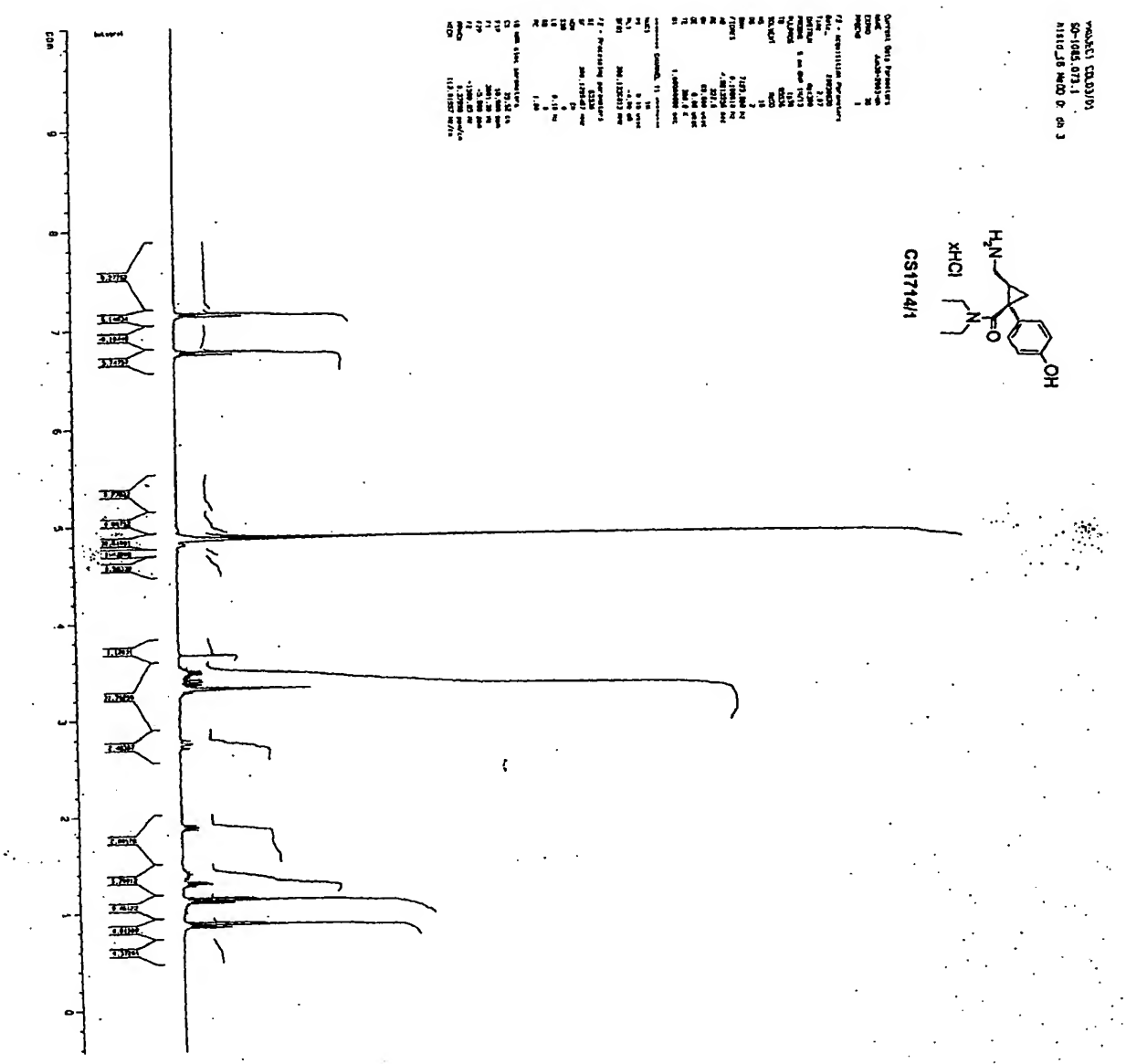


**Figure 25**

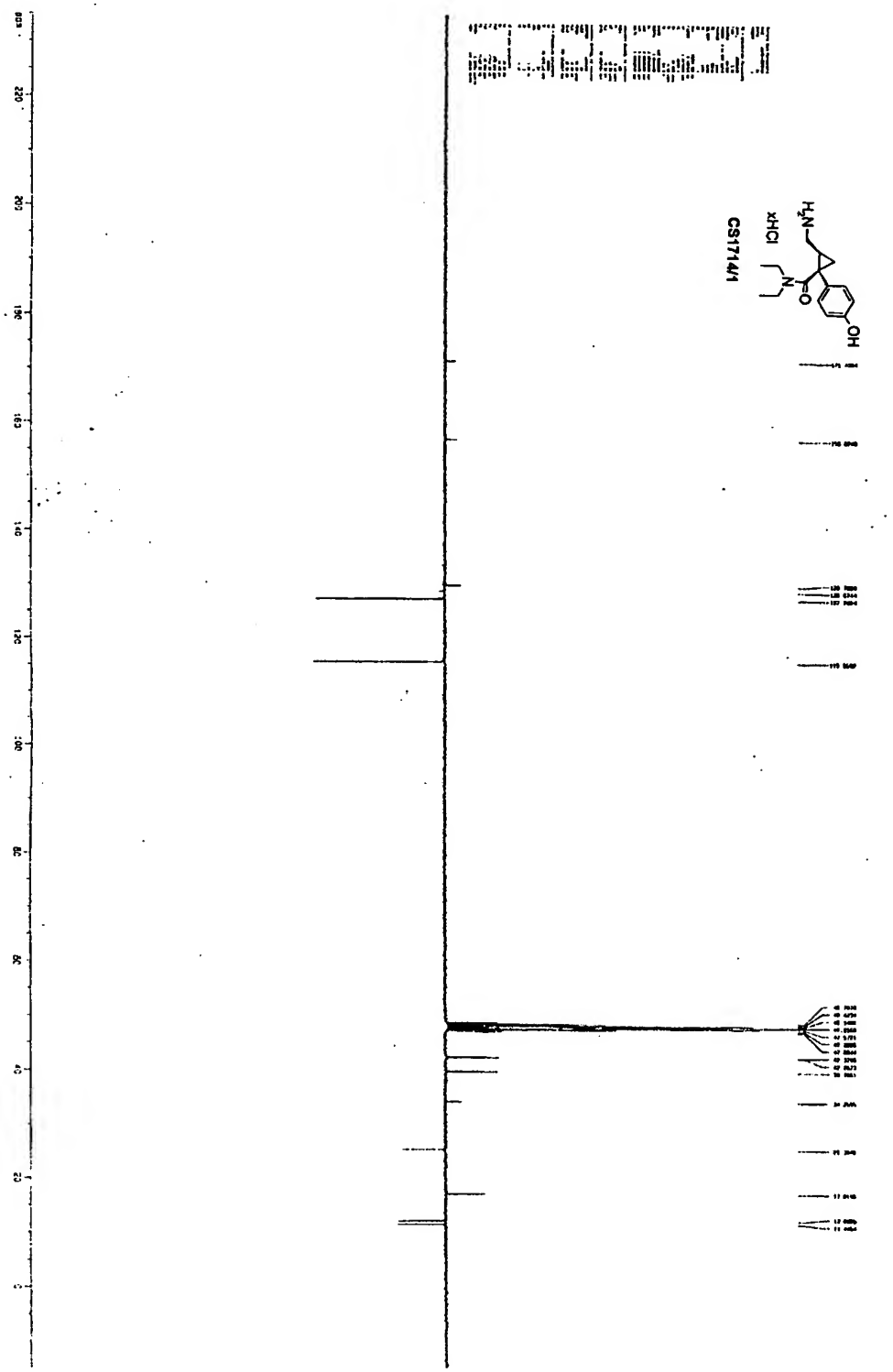


**Figure 26**

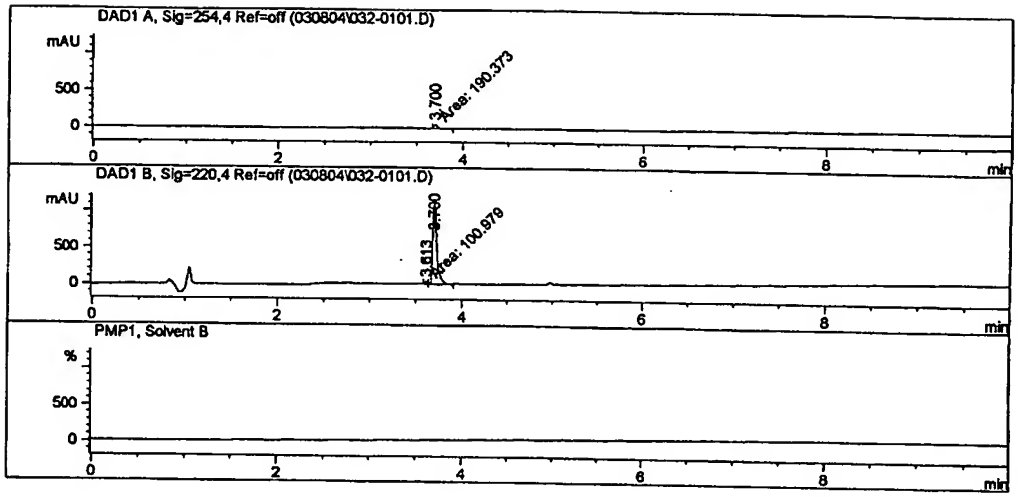

DAD1 A, Sig=254,4 Ref=off (030804\032-0101.D)
mAU
500
0
3.700
Area: 190.373
0
2
4
6
8
min
DAD1 B, Sig=220,4 Ref=off (030804\032-0101.D)
mAU
500
0
3.613
3.700
Area: 100.979
0
2
4
6
8
min
PMP1, Solvent B
%
500
0
0
2
4
6
8
min

**Figure 27**

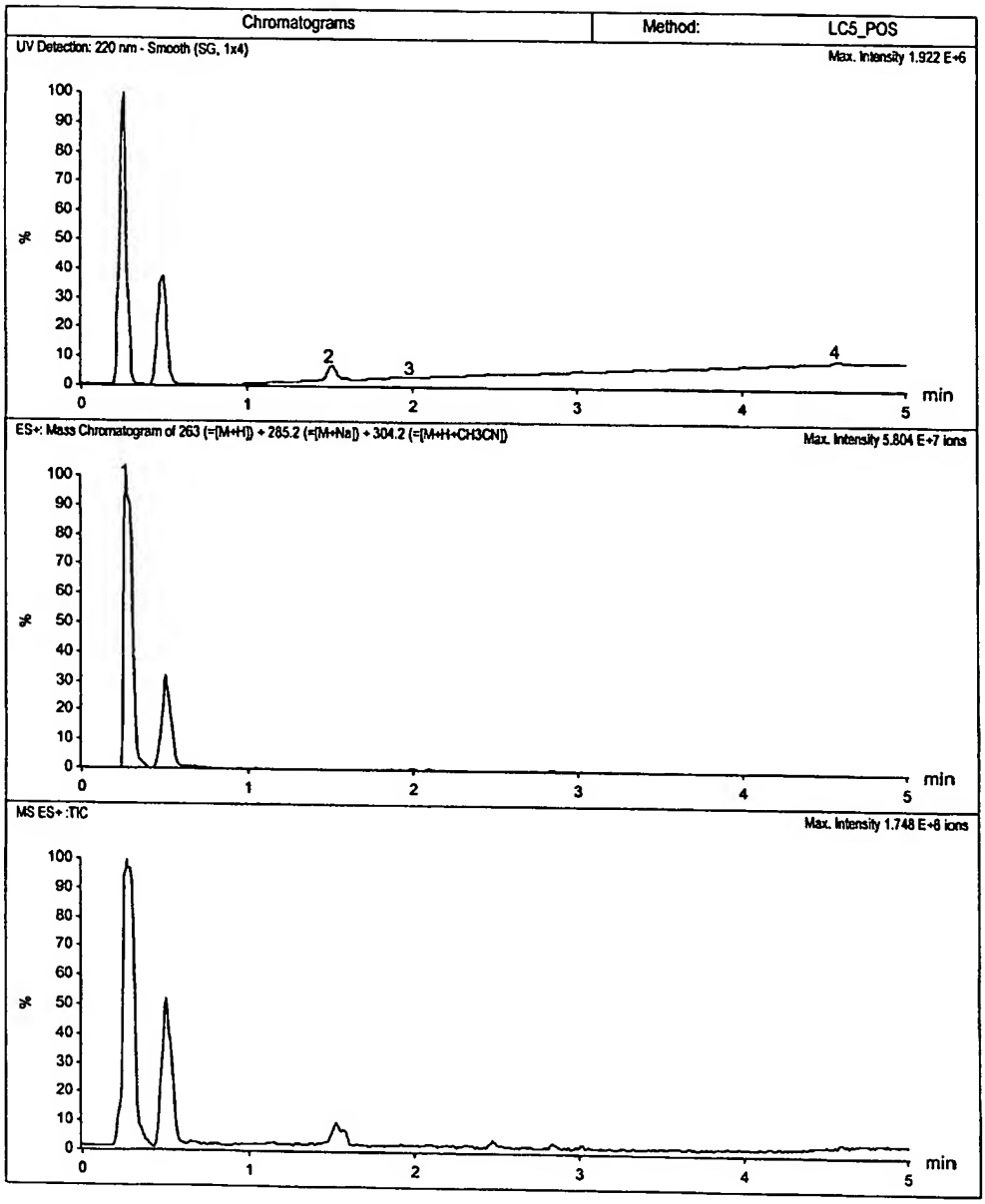

Chromatograms
Method: LC5_POS
UV Detection: 220 nm - Smooth (SG, 1x4)
Max. Intensity 1.922 E+6
%
min
2
3
4
ES+: Mass Chromatogram of 263 (=[M+H]) + 285.2 (=[M+Na]) + 304.2 (=[M+H+CH3CN])
Max. Intensity 5.804 E+7 ions
1
MS ES+ :TIC
Max. Intensity 1.748 E+8 ions

**Figure 28**

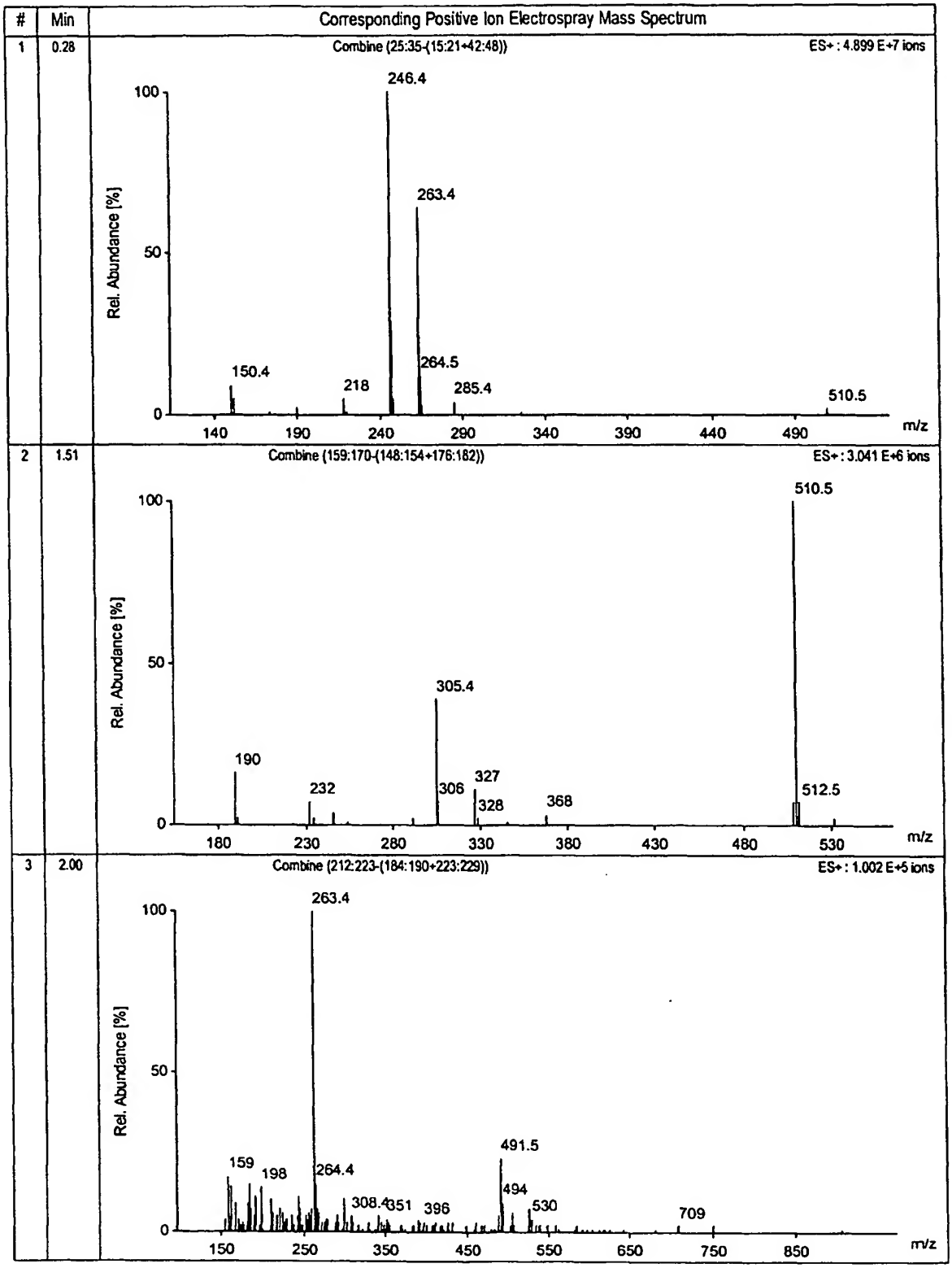

#
Min
Corresponding Positive Ion Electrospray Mass Spectrum
1
0.28
Combine (25:35-(15:21+42:48))
ES+ : 4.899 E+7 ions
246.4
263.4
264.5
150.4
218
285.4
510.5
Rel. Abundance [%]
m/z
2
1.51
Combine (159:170-(148:154+176:182))
ES+ : 3.041 E+6 ions
510.5
305.4
190
232
306
327
328
368
512.5
Rel. Abundance [%]
m/z
3
2.00
Combine (212:223-(184:190+223:229))
ES+ : 1.002 E+5 ions
263.4
491.5
159
198
264.4
308.4
351
396
494
530
709
Rel. Abundance [%]
m/z

**Figure 29**

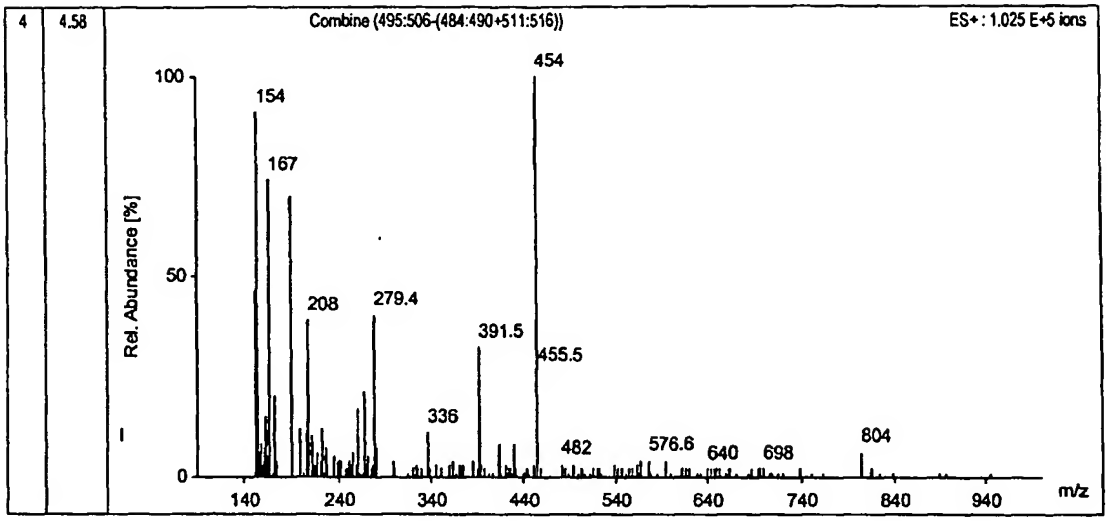

4
4.58
Combine (495:506-(484:490+511:516))
ES+: 1.025 E+5 ions
Rel. Abundance [%]
100
50
0
154
167
208
279.4
336
391.5
454
455.5
482
576.6
640
698
804
140
240
340
440
540
640
740
840
940
m/z

**Figure 30**

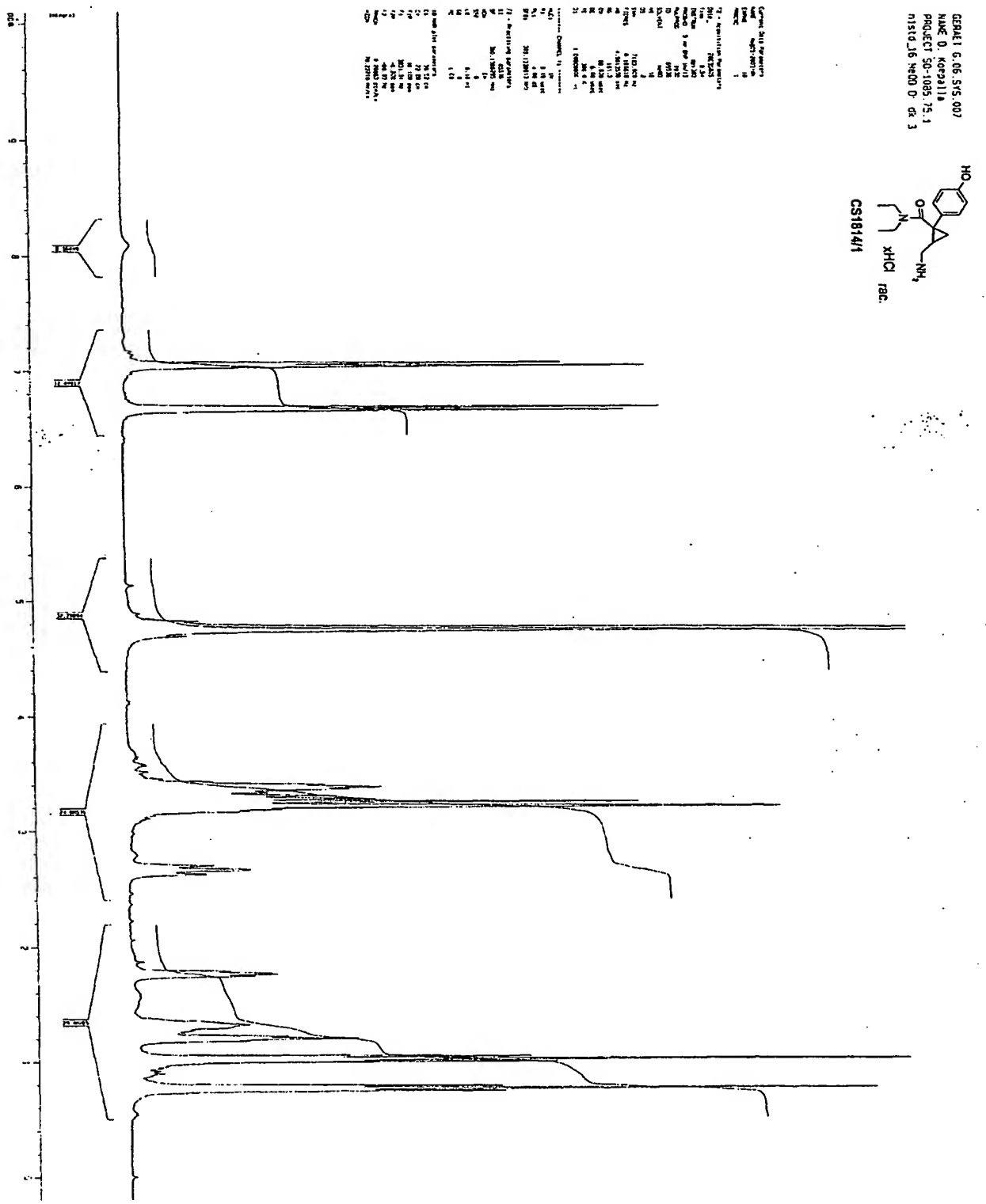
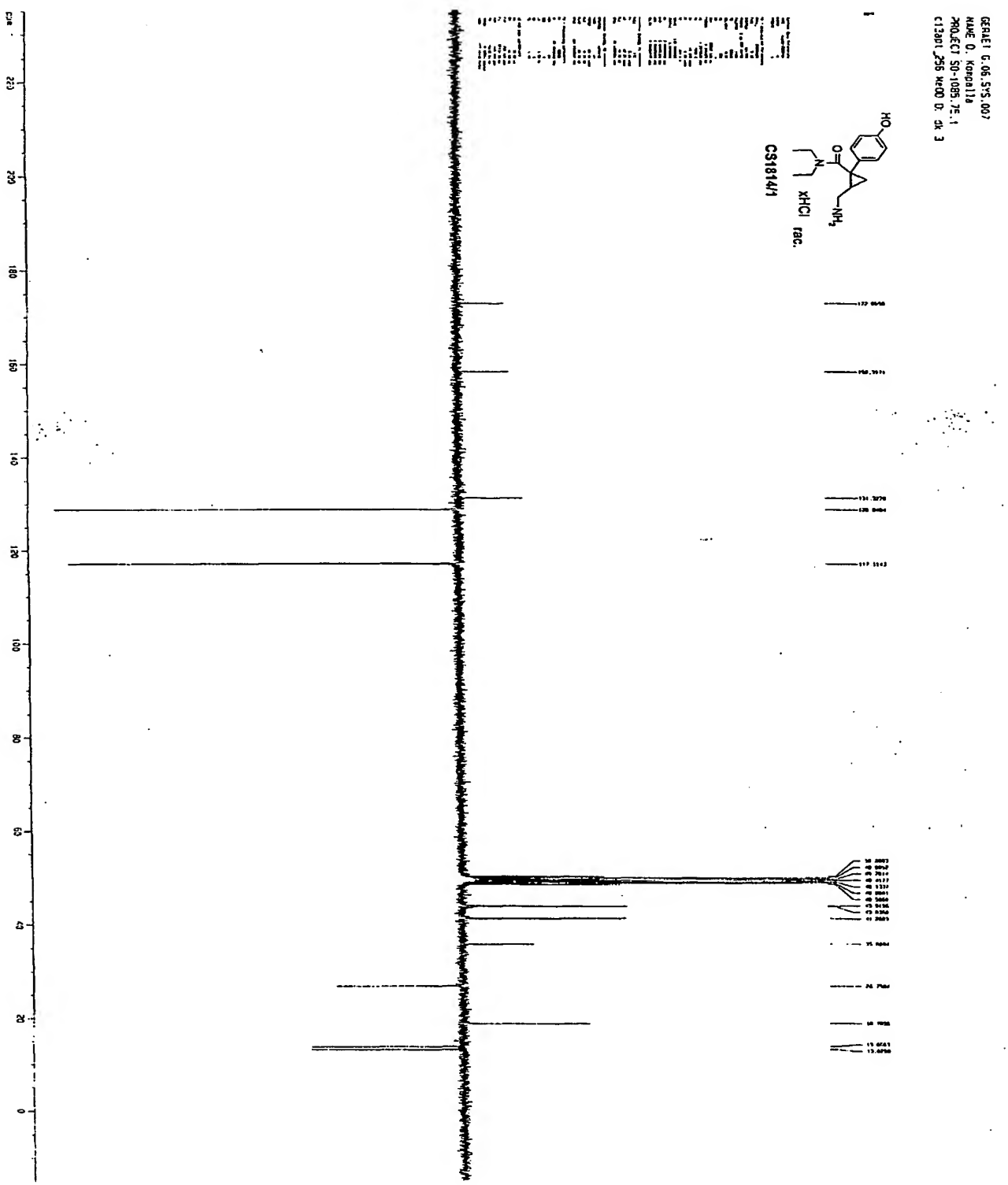

GERAET G.06.575.007
NAME D. Korpalla
PROJECT 50-1085.75.1
nistd_16 %d00 D dk 3
HO
O
N
NH2
xHCl
rac.
CS1814/1

**Figure 31**



## Figure 32

| CAT. # | TARGET | BATCH* | SPP. | n= | CONC. | †% INHIBITION -100 -50 0 50 100 % | $IC_{50}$ | $K_I$ | $n_H$ | R |
|---|---|---|---|---|---|---|---|---|---|---|
| 118050 | CYP450, 1A2 | 93172 | hum | 2 | 10 µM | 1 | | | | |
| 118070 | CYP450, 2C19 | 93174 | hum | 2 | 10 µM | 13 | | | | |
| 118060 | CYP450, 2C9 | 93173 | hum | 2 | 10 µM | 7 | | | | |
| 118080 | CYP450, 2D6 | 93175 | hum | 2 | 10 µM | 16 | | | | |
| 118090 | CYP450, 3A4 | 92943 | hum | 2 | 10 µM | 21 | | | | |
| 200510 | Adenosine $A_1$ | 92728 | hum | 2 | 10 µM | -5 | | | | |
| 200610 | Adenosine $A_{2A}$ | 92729 | hum | 2 | 10 µM | -2 | | | | |
| 203100 | Adrenergic $\alpha_{1A}$ | 92918 | rat | 2 | 10 µM | 16 | | | | |
| 203200 | Adrenergic $\alpha_{1B}$ | 92919 | rat | 2 | 10 µM | 5 | | | | |
| 203400 | Adrenergic $\alpha_{1D}$ | 92920 | hum | 2 | 10 µM | 10 | | | | |
| 203620 | Adrenergic $\alpha_{2A}$ | 92621 | hum | 2 | 10 µM | 15 | | | | |
| 203710 | Adrenergic $\alpha_{2B}$ | 92922 | hum | 2 | 10 µM | 14 | | | | |
| 204010 | Adrenergic $\beta_1$ | 92731 | hum | 2 | 10 µM | 8 | | | | |
| 204110 | Adrenergic $\beta_2$ | 92732 | hum | 2 | 10 µM | 3 | | | | |
| 212500 | Bradykinin $B_1$ | 92644 | hum | 2 | 10 µM | 10 | | | | |
| 212610 | Bradykinin $B_2$ | 92828 | hum | 2 | 10 µM | 20 | | | | |
| 214510 | Calcium Channel L-Type, Benzothiazepine | 92613 | rat | 2 | 10 µM | 26 | | | | |
| 214600 | Calcium Channel L-Type, Dihydropyridine | 92614 | rat | 2 | 10 µM | -14 | | | | |
| 216000 | Calcium Channel N-Type | 92708 | rat | 2 | 10 µM | -5 | | | | |
| 219500 | Dopamine $D_1$ | 92810 | hum | 2 | 10 µM | -4 | | | | |
| 219600 | Dopamine $D_{2L}$ | 92811 | hum | 2 | 10 µM | -4 | | | | |
| 219800 | Dopamine $D_3$ | 92813 | hum | 2 | 10 µM | -11 | | | | |
| 219900 | Dopamine $D_{4.2}$ | 92814 | hum | 2 | 10 µM | -1 | | | | |
| 224010 | Endothelin $ET_A$ | 92735 | hum | 2 | 10 µM | 0 | | | | |
| 224110 | Endothelin $ET_B$ | 92736 | hum | 2 | 10 µM | -5 | | | | |
| 225500 | Epidermal Growth Factor (EGF) | 92641 | hum | 2 | 10 µM | 3 | | | | |
| 226010 | Estrogen ERα | 92633 | hum | 2 | 10 µM | 7 | | | | |
| 226500 | $GABA_A$, Agonist Site | 92616 | rat | 2 | 10 µM | -10 | | | | |
| 226600 | $GABA_A$, Benzodiazepine, Central | 92830 | rat | 2 | 10 µM | -3 | | | | |
| 228510 | $GABA_B$, Non-Selective | 92715 | rat | 2 | 10 µM | 9 | | | | |
| 232010 | Glucocorticoid | 92894 | hum | 2 | 10 µM | 0 | | | | |

*Batch: Represents compounds tested concurrently in the same assay(s).

†Results with ≥ 50% stimulation or inhibition are boldfaced. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hum=human; syh=syrian hamster

## Figure 33

| CAT. # | TARGET | BATCH* | SPP. | n= | CONC. | †% INHIBITION -100 -50 0 50 100 % | $IC_{50}$ | $K_i$ | $n_H$ | R |
|---|---|---|---|---|---|---|---|---|---|---|
| 232700 | Glutamate, Kainate | 92635 | rat | 2 | 10 µM | 4 | | | | |
| 232810 | Glutamate, NMDA, Agonism | 92720 | rat | 2 | 10 µM | -10 | | | | |
| 232910 | Glutamate, NMDA, Glycine | 92912 | rat | 2 | 10 µM | 5 | | | | |
| 233000 | Glutamate, NMDA, Phencyclidine | 92636 | rat | 2 | 10 µM | 0 | | | | |
| 239610 | Histamine $H_1$ | 92617 | hum | 2 | 10 µM | -16 | | | | |
| 239710 | Histamine $H_2$ | 92618 | hum | 2 | 10 µM | 1 | | | | |
| 239810 | Histamine $H_3$ | 92853 | hum | 2 | 10 µM | -7 | | | | |
| 241000 | Imidazoline $I_2$, Central | 92836 | rat | 2 | 10 µM | -7 | | | | |
| 243510 | Interleukin IL-1, Non-Selective | 92929 | mous | 2 | 10 µM | 0 | | | | |
| 250600 | Leukotriene $LTD_4$ | 92643 | gp | 2 | 10 µM | -1 | | | | |
| 252600 | Muscarinic $M_1$ | 92840 | hum | 2 | 10 µM | 2 | | | | |
| 252700 | Muscarinic $M_2$ | 92841 | hum | 2 | 10 µM | 7 | | | | |
| 252800 | Muscarinic $M_3$ | 92842 | hum | 2 | 10 µM | -2 | | | | |
| 257000 | Neuropeptide $Y_1$ | 92820 | hum | 2 | 10 µM | 10 | | | | |
| 257110 | Neuropeptide $Y_2$ | 92821 | hum | 2 | 10 µM | 4 | | | | |
| 258590 | Nicotinic Acetylcholine | 92737 | hum | 2 | 10 µM | 5 | | | | |
| 260110 | Opiate δ (OP1, DOP) | 92824 | hum | 2 | 10 µM | -12 | | | | |
| 260210 | Opiate κ (OP2, KOP) | 92823 | hum | 2 | 10 µM | 6 | | | | |
| 260410 | Opiate µ (OP3, MOP) | 92822 | hum | 2 | 10 µM | -8 | | | | |
| 264500 | Phorbol Ester | 92834 | mous | 2 | 10 µM | 3 | | | | |
| 265010 | Platelet Activating Factor (PAF) | 92835 | hum | 2 | 10 µM | 3 | | | | |
| 265600 | Potassium Channel [$K_{ATP}$] | 92637 | syh | 2 | 10 µM | 9 | | | | |
| 268700 | Purinergic $P_{2X}$ | 92638 | rabbi | 2 | 10 µM | -1 | | | | |
| 268810 | Purinergic $P_{2Y}$ | 92649 | rat | 2 | 10 µM | -1 | | | | |
| 271110 | Serotonin (5-Hydroxytryptamine) 5-$HT_{1A}$ | 92716 | hum | 2 | 10 µM | -1 | | | | |
| 271910 | Serotonin (5-Hydroxytryptamine) 5-$HT_3$ | 92629 | hum | 2 | 10 µM | -1 | | | | |
| 278110 | Sigma $\sigma_1$ | 92925 | hum | 2 | 10 µM | 16 | | | | |
| 278200 | Sigma $\sigma_2$ | 92926 | rat | 2 | 10 µM | 1 | | | | |
| 279450 | Sodium Channel, Site 1 | 92838 | rat | 2 | 10 µM | 0 | | | | |
| 279510 | Sodium Channel, Site 2 | 92619 | rat | 2 | 10 µM | 5 | | | | |

*Batch: Represents compounds tested concurrently in the same assay(s).

†Results with ≥ 50% stimulation or inhibition are boldfaced. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hum=human; syh=syrian hamster

## Figure 34

| | CAT. # | TARGET | BATCH* | SPP. | n= | CONC. | †% INHIBITION | IC50 | Ki | nH | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | -100 -50 0 50 100 | | | | |
| | | | | | | | % ↓ ↓ ↓ ↓ ↓ | | | | |
| | 255510 | Tachykinin $NK_1$ | 92831 | hum | 2 | 10 µM | -10 | | | | |
| | 285010 | Testosterone | 93005 | rat | 2 | 10 µM | 8 | | | | |
| | 220320 | Transporter, Dopamine (DAT) | 92605 | hum | 2 | 10 µM | 9 | | | | |
| | 226400 | Transporter, GABA | 92827 | rat | 2 | 10 µM | 0 | | | | |
| | 204410 | Transporter, Norepinephrine (NET) | 92606 | hum | 2 | 10 µM | 86 | | | | |
| ♦ | | | 93798 | hum | 2 | 30 µM | 97 | 0.203 µM | 0.201 µM | 0.733 | |
| ♦ | | | | | 2 | 10 µM | 94 | | | | |
| ♦ | | | | | 2 | 3 µM | 90 | | | | |
| ♦ | | | | | 2 | 1 µM | 77 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 55 | | | | |
| | | | | | 2 | 0.1 µM | 39 | | | | |
| ♦ | | | 94109 | hum | 2 | 3 µM | 84 | 0.237 µM | 0.235 µM | 0.706 | |
| ♦ | | | | | 2 | 1 µM | 73 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 55 | | | | |
| | | | | | 2 | 0.1 µM | 37 | | | | |
| | | | | | 2 | 0.03 µM | 16 | | | | |
| ♦ | | | 94317 | hum | 2 | 3 µM | 86 | 0.22 µM | 0.218 µM | 0.596 | |
| ♦ | | | | | 2 | 1 µM | 71 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 51 | | | | |
| | | | | | 2 | 0.1 µM | 38 | | | | |
| | | | | | 2 | 0.03 µM | 26 | | | | |
| | 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | 92602 | hum | 2 | 10 µM | 99 | | | | |
| ♦ | | | 93802 | hum | 2 | 1 µM | 96 | 0.0139 µM | 7.4 nM | 0.704 | |
| ♦ | | | | | 2 | 0.3 µM | 87 | | | | |
| ♦ | | | | | 2 | 0.1 µM | 85 | | | | |
| ♦ | | | | | 2 | 0.03 µM | 63 | | | | |
| | | | | | 2 | 10 nM | 38 | | | | |
| | | | | | 2 | 3 nM | 30 | | | | |
| ♦ | | | 94111 | hum | 2 | 0.1 µM | 89 | 0.0111 µM | 5.89 nM | 0.864 | |
| ♦ | | | | | 2 | 0.03 µM | 70 | | | | |
| | | | | | 2 | 10 nM | 48 | | | | |
| | | | | | 2 | 3 nM | 21 | | | | |
| | | | | | 2 | 1 nM | 17 | | | | |

*Batch: Represents compounds tested concurrently in the same assay(s).

♦ Denotes item meeting criteria for significance

†Results with ≥ 50% stimulation or inhibition are boldfaced. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hum=human; syh=syrian hamster

**Figure 35**

| | CAT. # | TARGET | BATCH* | SPP. | n= | CONC. | †% INHIBITION -100 -50 0 50 100 % | $IC_{50}$ | $K_I$ | $n_H$ | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 274020 | Transporter, Serotonin (5- | | | | | | | | | |
| ◆ | | Hydroxytryptamine) (SERT) | 94318 | hum | 2 | 0.1 µM | 88 | 0.013 µM | 6.91 nM | 0.906 | |
| ◆ | | | | | 2 | 0.03 µM | 69 | | | | |
| | | | | | 2 | 10 nM | 42 | | | | |
| | | | | | 2 | 3 nM | 18 | | | | |
| | | | | | 2 | 1 nM | 15 | | | | |

*Batch: Represents compounds tested concurrently in the same assay(s).

◆ Denotes item meeting criteria for significance

†Results with ≥ 50% stimulation or inhibition are boldfaced. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hum=human; syh=syrian hamster

## Figure 36

| CAT. # | ASSAY NAME | REFERENCE COMPOUND | HISTORICAL $IC_{50}$ | HISTORICAL $K_I$ | HISTORICAL $n_H$ | CONCURRENT MIC BATCH* | CONCURRENT MIC $IC_{50}$ |
|---|---|---|---|---|---|---|---|
| 118050 | CYP450, 1A2 | Furafylline | 0.96 µM | | | 93172 | 0.835 µM |
| 118070 | CYP450, 2C19 | Tranylcypromine | 8.1 µM | | | 93174 | 8.68 µM |
| 118060 | CYP450, 2C9 | Sulfaphenazole | 0.77 µM | | | 93173 | 0.453 µM |
| 118080 | CYP450, 2D6 | Quinidine | 0.057 µM | | | 93175 | 0.0368 µM |
| 118090 | CYP450, 3A4 | Ketoconazole | 0.22 µM | | | 92943 | 0.263 µM |
| 200510 | Adenosine $A_1$ | R(-)-PIA | 0.44 µM | 0.26 µM | 0.8 | 92728 | 0.549 µM |
| 200610 | Adenosine $A_{2A}$ | CGS-21680 | 0.46 µM | 0.26 µM | 0.9 | 92729 | 0.118 µM |
| 203100 | Adrenergic $\alpha_{1A}$ | Prazosin | 0.69 nM | 0.28 nM | 0.9 | 92918 | 0.385 nM |
| 203200 | Adrenergic $\alpha_{1B}$ | Prazosin | 0.27 nM | 0.15 nM | 1 | 92919 | 0.238 nM |
| 203400 | Adrenergic $\alpha_{1D}$ | Prazosin | 0.88 nM | 0.43 nM | 0.7 | 92920 | 0.595 nM |
| 203620 | Adrenergic $\alpha_{2A}$ | Yohimbine | 8.4 nM | 3.1 nM | 0.9 | 92621 | 3.35 nM |
| 203710 | Adrenergic $\alpha_{2B}$ | Yohimbine | 0.014 µM | 6.4 nM | 1 | 92922 | 0.0341 µM |
| 204010 | Adrenergic $\beta_1$ | S(-)-Propranolol | 2.5 nM | 1.4 nM | 0.8 | 92731 | 1.91 nM |
| 204110 | Adrenergic $\beta_2$ | S(-)-Propranolol | 0.78 nM | 0.54 nM | 1.2 | 92732 | 0.448 nM |
| 212500 | Bradykinin $B_1$ | (Des-Arg$^{10}$)-Kallidin | 1.6 nM | 0.27 nM | 0.9 | 92644 | 2 nM |
| 212610 | Bradykinin $B_2$ | Bradykinin | 0.89 nM | 0.53 nM | 0.9 | 92828 | 0.897 nM |
| 214510 | Calcium Channel L-Type, Benzothiazepine | Diltiazem | 0.036 µM | 0.032 µM | 0.9 | 92613 | 0.0337 µM |
| 214600 | Calcium Channel L-Type, Dihydropyridine | Nitrendipine | 0.72 nM | 0.46 nM | 0.9 | 92614 | 1.31 nM |
| 216000 | Calcium Channel N-Type | ω-Conotoxin GVIA | 0.034 nM | 0.028 nM | 1.6 | 92708 | 0.0117 nM |
| 219500 | Dopamine $D_1$ | R(+)-SCH-23390 | 1.4 nM | 0.7 nM | 0.9 | 92810 | 1.48 nM |
| 219600 | Dopamine $D_{2L}$ | Spiperone | 0.58 nM | 0.19 nM | 1.2 | 92811 | 0.356 nM |
| 219800 | Dopamine $D_3$ | Spiperone | 0.36 nM | 0.12 nM | 0.9 | 92813 | 0.73 nM |
| 219900 | Dopamine $D_{4.2}$ | Spiperone | 0.98 nM | 0.34 nM | 1 | 92814 | 1.87 nM |
| 224010 | Endothelin $ET_A$ | Endothelin-1 | 0.23 nM | 0.14 nM | 1.1 | 92735 | 0.327 nM |
| 224110 | Endothelin $ET_B$ | Endothelin-1 | 0.13 nM | 0.06 nM | 0.9 | 92736 | 0.0785 nM |
| 225500 | Epidermal Growth Factor (EGF) | Epidermal Growth Factor (EGF) (human) | 0.39 nM | 0.15 nM | 1.2 | 92641 | 0.169 nM |
| 226010 | Estrogen ERα | Diethylstilbestrol | 1.1 nM | 0.31 nM | 1.1 | 92633 | 0.52 nM |
| 226500 | $GABA_A$, Agonist Site | GABA | 0.08 µM | 0.063 µM | 0.8 | 92616 | 0.0641 µM |
| 226600 | $GABA_A$, Benzodiazepine, Central | Diazepam | 0.016 µM | 0.013 µM | 0.8 | 92830 | 0.011 µM |
| 228510 | $GABA_B$, Non-Selective | CGP-54626 | 1.8 nM | 1.4 nM | 1 | 92715 | 1.96 nM |
| 232010 | Glucocorticoid | Dexamethasone | 0.041 µM | 0.019 µM | 0.9 | 92894 | 9.03 nM |
| 232700 | Glutamate, Kainate | L-Glutamate | 0.24 µM | 0.17 µM | 0.8 | 92635 | 0.272 µM |
| 232810 | Glutamate, NMDA, Agonism | L-Glutamate | 0.41 µM | 0.37 µM | 0.9 | 92720 | 0.303 µM |
| 232910 | Glutamate, NMDA, Glycine | MDL-105519 | 0.022 µM | 0.021 µM | 0.6 | 92912 | 5.28 nM |
| 233000 | Glutamate, NMDA, Phencyclidine | Dizolcipine (MK-801) | 5.1 nM | 3.4 nM | 0.7 | 92636 | 5.42 nM |

*Batch: Represents compounds tested concurrently in the same assay(s).

## Figure 37

| CAT. # | ASSAY NAME | REFERENCE COMPOUND | HISTORICAL | | | CONCURRENT MIC | |
|---|---|---|---|---|---|---|---|
| | | | $IC_{50}$ | $K_i$ | $n_H$ | BATCH* | $IC_{50}$ |
| 239610 | Histamine $H_1$ | Pyrilamine | 3.3 nM | 1.6 nM | 1 | 92617 | 3.32 nM |
| 239710 | Histamine $H_2$ | Tiotidine | 0.022 µM | 0.018 µM | 1.1 | 92618 | 0.028 µM |
| 239810 | Histamine $H_3$ | R(-)-α-Methylhistamine (RAMH) | 5.2 nM | 2.3 nM | 0.9 | 92853 | 4.6 nM |
| 241000 | Imidazoline $I_2$, Central | Idazoxan | 0.012 µM | 8 nM | 1 | 92836 | 6.93 nM |
| 243510 | Interleukin IL-1, Non-Selective | Interleukin-1α (IL-1α) | 0.027 nM | 10 pM | 1 | 92929 | 0.0417 nM |
| 250600 | Leukotriene $LTD_4$ | Leukotriene $D_4$ ($LTD_4$) | 1.4 nM | 0.7 nM | 1 | 92643 | 0.731 nM |
| 252600 | Muscarinic $M_1$ | 4-DAMP | 4.3 nM | 1 nM | 1 | 92840 | 3.82 nM |
| 252700 | Muscarinic $M_2$ | 4-DAMP | 0.013 µM | 4.6 nM | 0.9 | 92841 | 0.0219 µM |
| 252800 | Muscarinic $M_3$ | 4-DAMP | 3.9 nM | 0.83 nM | 1 | 92842 | 3.21 nM |
| 257000 | Neuropeptide $Y_1$ | Neuropeptide Y (human, rat) | 4 nM | 3.9 nM | 1 | 92820 | 1.06 nM |
| 257110 | Neuropeptide $Y_2$ | Neuropeptide Y (13-36) (porcine) | 4.4 nM | 2.4 nM | 0.7 | 92821 | 2.28 nM |
| 258590 | Nicotinic Acetylcholine | (+)-Epibatidine | 0.071 nM | 0.049 µM | 0.9 | 92737 | 0.0545 nM |
| 260110 | Opiate δ (OP1, DOP) | Naltrindole | 0.92 nM | 0.32 nM | 1 | 92824 | 0.85 nM |
| 260210 | Opiate κ (OP2, KOP) | U-69593 | 0.016 µM | 6.4 nM | 0.5 | 92823 | 7.68 nM |
| 260410 | Opiate µ (OP3, MOP) | DAMGO | 0.02 µM | 8.1 nM | 0.6 | 92822 | 0.011 µM |
| 264500 | Phorbol Ester | PMA | 9.1 nM | 6.8 nM | 1.1 | 92834 | 9.95 nM |
| 265010 | Platelet Activating Factor (PAF) | PAF | 0.28 nM | 0.15 nM | 0.9 | 92835 | 0.548 nM |
| 265600 | Potassium Channel [$K_{ATP}$] | Glyburide | 0.018 µM | 2 nM | 0.8 | 92637 | 8.04 nM |
| 268700 | Purinergic $P_{2X}$ | α, β-Methylene ATP | 0.082 µM | 0.018 µM | 1.1 | 92638 | 0.0764 µM |
| 268810 | Purinergic $P_{2Y}$ | ATP | 0.018 µM | 0.018 µM | 0.9 | 92649 | 0.038 µM |
| 271110 | Serotonin (5-Hydroxytryptamine) 5-$HT_{1A}$ | Metergoline | 4.1 nM | 2.3 nM | 0.9 | 92716 | 6.6 nM |
| 271910 | Serotonin (5-Hydroxytryptamine) 5-$HT_3$ | MDL-72222 | 0.011 µM | 2.5 nM | 0.8 | 92629 | 0.0157 µM |
| 278110 | Sigma $\sigma_1$ | Haloperidol | 0.021 µM | 8.8 nM | 0.9 | 92925 | 7.67 nM |
| 278200 | Sigma $\sigma_2$ | Ifenprodil | 8 nM | 4.9 nM | 0.7 | 92926 | 3.55 nM |
| 279450 | Sodium Channel, Site 1 | Saxitoxin | 1.7 nM | 0.7 nM | 1 | 92838 | 2.31 nM |
| 279510 | Sodium Channel, Site 2 | Dibucaine | 0.61 µM | 0.55 µM | 0.9 | 92619 | 0.892 µM |
| 255510 | Tachykinin $NK_1$ | L-703,606 | 0.025 µM | 0.014 µM | 0.8 | 92831 | 0.0217 µM |
| 285010 | Testosterone | Testosterone | 6.5 nM | 4.3 nM | 1 | 93005 | 6.37 nM |
| 220320 | Transporter, Dopamine (DAT) | GBR-12909 | 1.7 nM | 1.3 nM | 0.9 | 92605 | 0.692 nM |
| 226400 | Transporter, GABA | NO-711 | 0.2 µM | 0.2 µM | 1.1 | 92827 | 0.214 µM |
| 204410 | Transporter, Norepinephrine (NET) | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 92606 | 0.83 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 93798 | 2.06 nM |

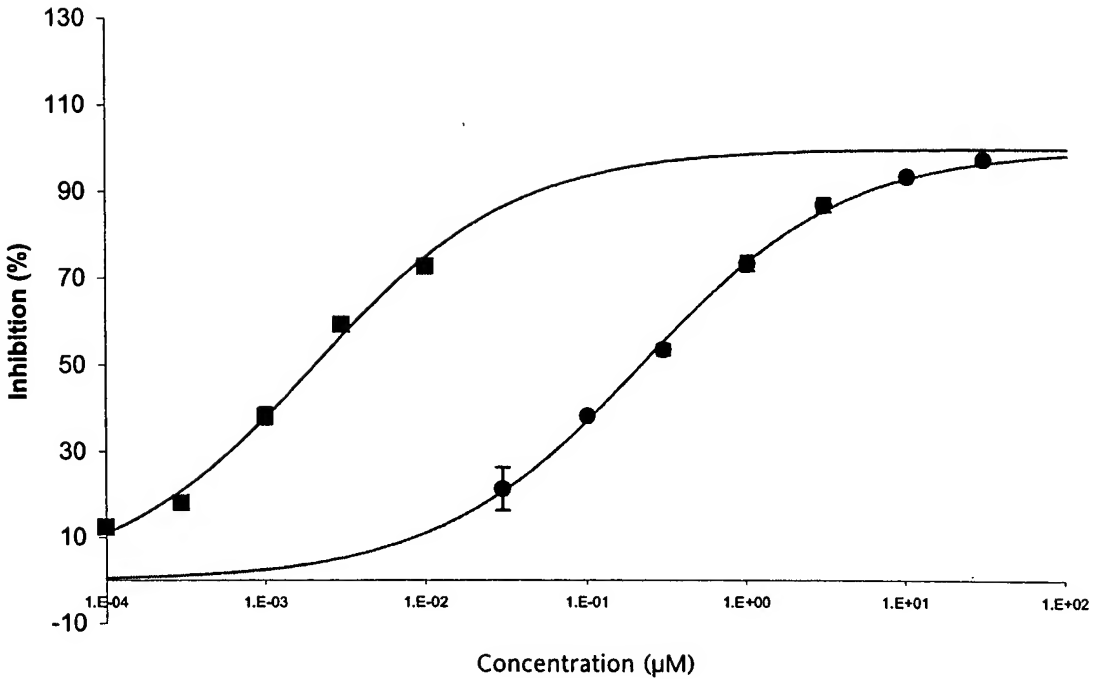
*Batch: Represents compounds tested concurrently in the same assay(s).

**Figure 38**

| CAT. # | ASSAY NAME | REFERENCE COMPOUND | HISTORICAL | | | CONCURRENT MIC | |
|---|---|---|---|---|---|---|---|
| | | | $IC_{50}$ | $K_i$ | $n_H$ | BATCH* | $IC_{50}$ |
| 204410 | Transporter, Norepinephrine (NET) | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 94109 | 2.13 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 94317 | 1.96 nM |
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | GBR-12909 | 0.11 μM | 0.057 μM | 0.8 | 92602 | 0.0667 μM |
| | | GBR-12909 | 0.11 μM | 0.057 μM | 0.8 | 93802 | 0.0941 μM |
| | | GBR-12909 | 0.11 μM | 0.057 μM | 0.8 | 94111 | 0.0671 μM |
| | | GBR-12909 | 0.11 μM | 0.057 μM | 0.8 | 94318 | 0.103 μM |

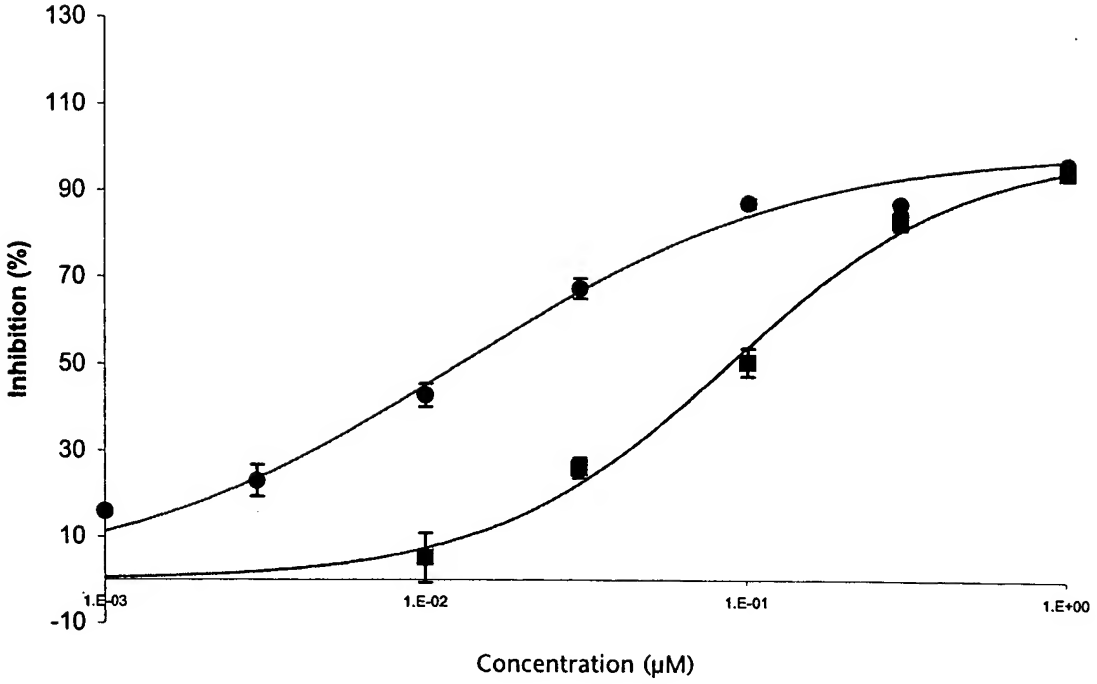
*Batch: Represents compounds tested concurrently in the same assay(s).

**Figure 39**




| Compound | $IC_{50}$ | $K_I$ | $n_H$ |
|---|---|---|---|
| Vial #1 (1036183) | 0.22 ± 0.01 µM | 0.218 ± 0.01 µM | 0.678 ± 0.042 |
| ■ Desipramine | 2.05 ± 0.049 nM | 2.03 ± 0.048 nM | 0.694 ± 0.036 |

**Figure 40**




| Compound | $IC_{50}$ | $K_I$ | $n_H$ |
|---|---|---|---|
| Vial #1 (1036183) | 0.0127 ± 0.001 μM | 6.73 ± 0.442 nM | 0.825 ± 0.0616 |
| ■ GBR-12909 | 0.088 ± 0.0107 μM | 0.0467 ± 0.006 μM | 1.17 ± 0.088 |

**Figure 41**

| | COMPOUND CODE | PT NUMBER | BATCH* | SPP. | n= | CONC. | †% INHIBITION % -100 -50 0 50 100 | $IC_{50}$ | $K_I$ | $n_H$ | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 212610 Bradykinin $B_2$ | | | | | | | | | | |
| | Vial # 2 | 1037044 | 94766 | hum | 2 | 10 µM | -15 | | | | |
| | Vial # 3 | 1037045 | 94766 | hum | 2 | 10 µM | -2 | | | | |
| | 118090 CYP450, 3A4 | | | | | | | | | | |
| | Vial # 2 | 1037044 | 95160 | hum | 2 | 10 µM | 24 | | | | |
| | Vial # 3 | 1037045 | 95160 | hum | 2 | 10 µM | 39 | | | | |
| | 214510 Calcium Channel L-Type, Benzothiazepine | | | | | | | | | | |
| | Vial # 2 | 1037044 | 94767 | rat | 2 | 10 µM | 26 | | | | |
| | Vial # 3 | 1037045 | 94767 | rat | 2 | 10 µM | 34 | | | | |
| | 204410 Transporter, Norepinephrine (NET) | | | | | | | | | | |
| ♦ | Vial # 2 | 1037044 | 94760 | hum | 2 | 10 µM | 92 | | | | |
| ♦ | | | 95109 | hum | 2 | 3 µM | 85 | 0.0978 µM | 0.097 µM | 0.62 | |
| ♦ | | | | | 2 | 1 µM | 82 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 63 | | | | |
| ♦ | | | | | 2 | 0.1 µM | 59 | | | | |
| | | | | | 2 | 0.03 µM | 30 | | | | |
| | | | | | 2 | 10 nM | 16 | | | | |
| ♦ | | | 95324 | hum | 2 | 3 µM | 86 | 0.101 µM | 0.1 µM | 0.493 | |
| ♦ | | | | | 2 | 1 µM | 74 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 63 | | | | |
| ♦ | | | | | 2 | 0.1 µM | 51 | | | | |
| | | | | | 2 | 0.03 µM | 35 | | | | |
| ♦ | | | 95371 | hum | 2 | 3 µM | 84 | 0.138 µM | 0.136 µM | 0.64 | |
| ♦ | | | | | 2 | 1 µM | 77 | | | | |
| ♦ | | | | | 2 | 0.3 µM | 66 | | | | |
| | | | | | 2 | 0.1 µM | 47 | | | | |
| | | | | | 2 | 0.03 µM | 23 | | | | |
| ♦ | Vial # 3 | 1037045 | 94760 | hum | 2 | 10 µM | 84 | | | | |
| ♦ | | | 94891 | hum | 2 | 30 µM | 87 | 1.67 µM | 1.65 µM | 0.745 | |
| ♦ | | | | | 2 | 10 µM | 78 | | | | |

* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)
R=Additional Comments
hum=human

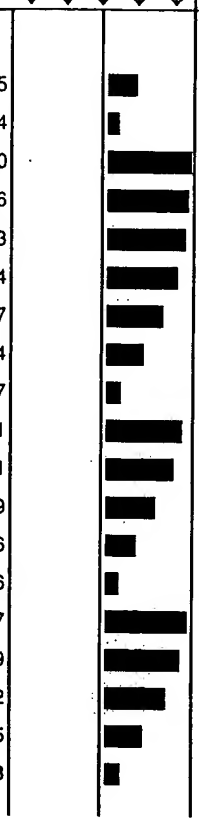
**Figure 42**

| | COMPOUND CODE | PT NUMBER | BATCH* | SPP. | n= | CONC. | †% INHIBITION % | -100 -50 0 50 100 | $IC_{50}$ | $K_I$ | $n_H$ | R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 204410 | Transporter, Norepinephrine (NET) | | | | | | | | | | | |
| ♦ | Vial # 3 | 1037045 | 94891 | hum | 2 | 3 µM | 61 | | 1.67 µM | 1.65 µM | 0.745 | |
| | | | | | 2 | 1 µM | 46 | | | | | |
| | | | | | 2 | 0.3 µM | 18 | | | | | |
| | | | | | 2 | 0.1 µM | 9 | | | | | |
| ♦ | | | 95109 | hum | 2 | 30 µM | 93 | | 1.43 µM | 1.42 µM | 0.77 | |
| ♦ | | | | | 2 | 10 µM | 77 | | | | | |
| ♦ | | | | | 2 | 3 µM | 66 | | | | | |
| | | | | | 2 | 1 µM | 45 | | | | | |
| | | | | | 2 | 0.3 µM | 21 | | | | | |
| ♦ | | | 95324 | hum | 2 | 30 µM | 78 | | 1.95 µM | 1.93 µM | 0.523 | |
| ♦ | | | | | 2 | 10 µM | 72 | | | | | |
| ♦ | | | | | 2 | 3 µM | 57 | | | | | |
| | | | | | 2 | 1 µM | 40 | | | | | |
| | | | | | 2 | 0.3 µM | 27 | | | | | |
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | | | | | | | | | | | |
| ♦ | Vial # 2 | 1037044 | 94762 | hum | 2 | 10 µM | 98 | | | | | |
| ♦ | | | 95110 | hum | 2 | 0.3 µM | 95 | | 7.17 nM | 3.81 nM | 0.999 | |
| ♦ | | | | | 2 | 0.1 µM | 93 | | | | | |
| ♦ | | | | | 2 | 0.03 µM | 80 | | | | | |
| ♦ | | | | | 2 | 10 nM | 59 | | | | | |
| | | | | | 2 | 3 nM | 31 | | | | | |
| | | | | | 2 | 1 nM | 10 | | | | | |
| ♦ | | | 95326 | hum | 2 | 0.1 µM | 88 | | 8.68 nM | 4.61 nM | 0.906 | |
| ♦ | | | | | 2 | 0.03 µM | 77 | | | | | |
| ♦ | | | | | 2 | 10 nM | 53 | | | | | |
| | | | | | 2 | 3 nM | 28 | | | | | |
| | | | | | 2 | 1 nM | 11 | | | | | |
| ♦ | | | 95372 | hum | 2 | 0.1 µM | 92 | | 6.03 nM | 3.2 nM | 0.942 | |
| ♦ | | | | | 2 | 0.03 µM | 82 | | | | | |
| ♦ | | | | | 2 | 10 nM | 62 | | | | | |

* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)
R=Additional Comments
hum=human

**Figure 43**

| | COMPOUND CODE | PT NUMBER | BATCH* | SPP. | n= | CONC. | †% INHIBITION % | IC50 | KI | nH | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 274020 Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | | | | | | | | | | |
| | Vial # 2 | 1037044 | 95372 | hum | 2 | 3 nM | 35 | 6.03 nM | 3.2 nM | 0.942 | |
| | | | | | 2 | 1 nM | 14 | | | | |
| ♦ | Vial # 3 | 1037045 | 94762 | hum | 2 | 10 µM | 100 | | | | |
| ♦ | | | 95110 | hum | 2 | 1 µM | 96 | 0.014 µM | 7.45 nM | 0.907 | |
| ♦ | | | | | 2 | 0.3 µM | 93 | | | | |
| ♦ | | | | | 2 | 0.1 µM | 84 | | | | |
| ♦ | | | | | 2 | 0.03 µM | 67 | | | | |
| | | | | | 2 | 10 nM | 44 | | | | |
| | | | | | 2 | 3 nM | 17 | | | | |
| ♦ | | | 95326 | hum | 2 | 0.3 µM | 91 | 0.0197 µM | 0.0105 µM | 0.869 | |
| ♦ | | | | | 2 | 0.1 µM | 81 | | | | |
| ♦ | | | | | 2 | 0.03 µM | 59 | | | | |
| | | | | | 2 | 10 nM | 36 | | | | |
| | | | | | 2 | 3 nM | 16 | | | | |
| ♦ | | | 95372 | hum | 2 | 0.3 µM | 97 | 0.0123 µM | 6.52 nM | 1.05 | |
| ♦ | | | | | 2 | 0.1 µM | 89 | | | | |
| ♦ | | | | | 2 | 0.03 µM | 72 | | | | |
| | | | | | 2 | 10 nM | 45 | | | | |
| | | | | | 2 | 3 nM | 18 | | | | |




* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)
R=Additional Comments
hum=human

**Figure 44**

## CELLULAR ASSAYS

| COMPOUND CODE | PT NUMBER | BATCH* | TISSUE, SPECIES | n= | CONC. | CRITERIA | %RESPONSE RESP. | AG. | ANT. | R |
|---|---|---|---|---|---|---|---|---|---|---|
| 302100 Cytotoxicity, Norepinephrine Uptake | | | | | | | | | | |
| Vial #1 | 1036183 | 95055 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | 9 | |
| Vial #1 | 1036183 | 95055 | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | 8 | |
| | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | -4 | |
| | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | 0 | |
| | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | -8 | |
| Vial # 2 | 1037044 | 95055 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | 11 | |
| | | | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | 14 | |
| | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 7 | |
| | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | 9 | |
| | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | 0 | |
| Vial # 3 | 1037045 | 95055 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | -6 | |
| | | | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | -1 | |
| | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | -6 | |
| | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | -6 | |
| | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | -3 | |
| 364100 Cytotoxicity, Serotonin (5-Hydroxytryptamine) Uptake | | | | | | | | | | |
| Vial #1 | 1036183 | 95056 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | 2 | |
| | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | -7 | |
| | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 0 | |
| | | | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | -2 | |
| | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | -3 | |
| Vial # 2 | 1037044 | 95056 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | -8 | |
| | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | -7 | |
| | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | -2 | |
| | | | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | 0 | |
| | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | 2 | |
| Vial # 3 | 1037045 | 95056 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | -3 | |
| | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | -6 | |
| | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | -6 | |

* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
Ag.=Agonist; Ant.=Antagonist; Resp.=Response; ND=Assay Test Not Done; R=Additional Comments
hum=human

**Figure 45**

## CELLULAR ASSAYS

| | COMPOUND CODE | PT NUMBER | BATCH* | TISSUE, SPECIES | n= | CONC. | CRITERIA | %RESPONSE RESP. | AG. | ANT. | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 364100 Cytotoxicity, Serotonin (5-Hydroxytryptamine) Uptake | | | | | | | | | | |
| | Vial # 3 | 1037045 | 95056 | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | -4 | |
| | | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | -1 | |
| | 302000 Uptake, Norepinephrine | | | | | | | | | | |
| ♦ | Vial #1 | 1036183 | 94864 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | 95 | |
| ♦ | | | | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | 95 | |
| ♦ | | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 78 | |
| | | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | 25 | |
| | | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | 7 | |
| ♦ | Vial # 2 | 1037044 | 94864 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | 99 | |
| ♦ | | | | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | 98 | |
| ♦ | | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 90 | |
| ♦ | | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | 50 | |
| | | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | 5 | |
| ♦ | Vial # 3 | 1037045 | 94864 | MDCK cells, hum | 2 | 10 µM | ≥ ± 50% | | | 97 | |
| ♦ | | | | MDCK cells, hum | 2 | 1 µM | ≥ ± 50% | | | 83 | |
| | | | | MDCK cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 48 | |
| | | | | MDCK cells, hum | 2 | 10 nM | ≥ ± 50% | | | 20 | |
| | | | | MDCK cells, hum | 2 | 1 nM | ≥ ± 50% | | | 15 | |
| | 364000 Uptake, Serotonin (5-Hydroxytryptamine) | | | | | | | | | | |
| ♦ | Vial #1 | 1036183 | 94865 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | 100 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | 94 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 75 | |
| | | | | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | 38 | |
| | | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | 4 | |
| ♦ | Vial # 2 | 1037044 | 94865 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | 99 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | 96 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 80 | |
| | | | | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | 33 | |
| | | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | 5 | |

* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
Ag.=Agonist; Ant.=Antagonist; Resp.=Response; ND=Assay Test Not Done; R=Additional Comments
hum=human

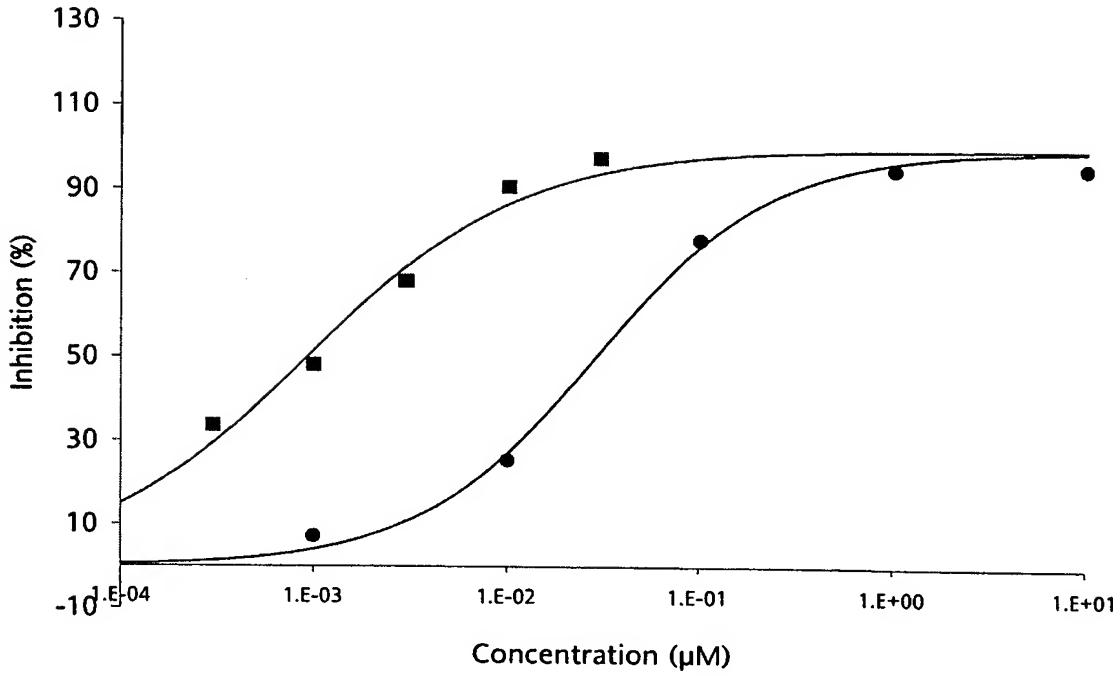
**Figure 46**

## CELLULAR ASSAYS

| | COMPOUND CODE | PT NUMBER | BATCH* | TISSUE, SPECIES | n= | CONC. | CRITERIA | %RESPONSE RESP. | AG. | ANT. | R |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 364000 Uptake, Serotonin (5-Hydroxytryptamine) | | | | | | | | | | |
| ♦ | Vial # 3 | 1037045 | 94865 | HEK-293 cells, hum | 2 | 10 µM | ≥ ± 50% | | | 100 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 1 µM | ≥ ± 50% | | | 88 | |
| ♦ | | | | HEK-293 cells, hum | 2 | 0.1 µM | ≥ ± 50% | | | 65 | |
| | | | | HEK-293 cells, hum | 2 | 10 nM | ≥ ± 50% | | | 33 | |
| | | | | HEK-293 cells, hum | 2 | 1 nM | ≥ ± 50% | | | -4 | |

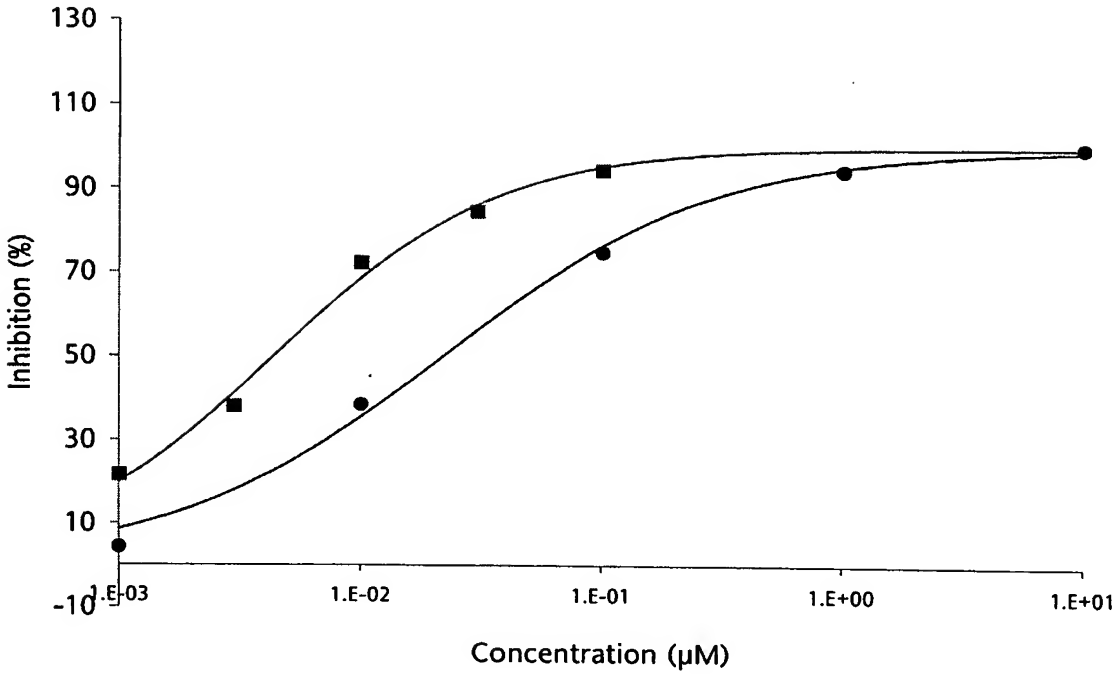
* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.
♦ Denotes item meeting criteria for significance
Ag.=Agonist; Ant.=Antagonist; Resp.=Response; ND=Assay Test Not Done; R=Additional Comments
hum=human

**Figure 47**



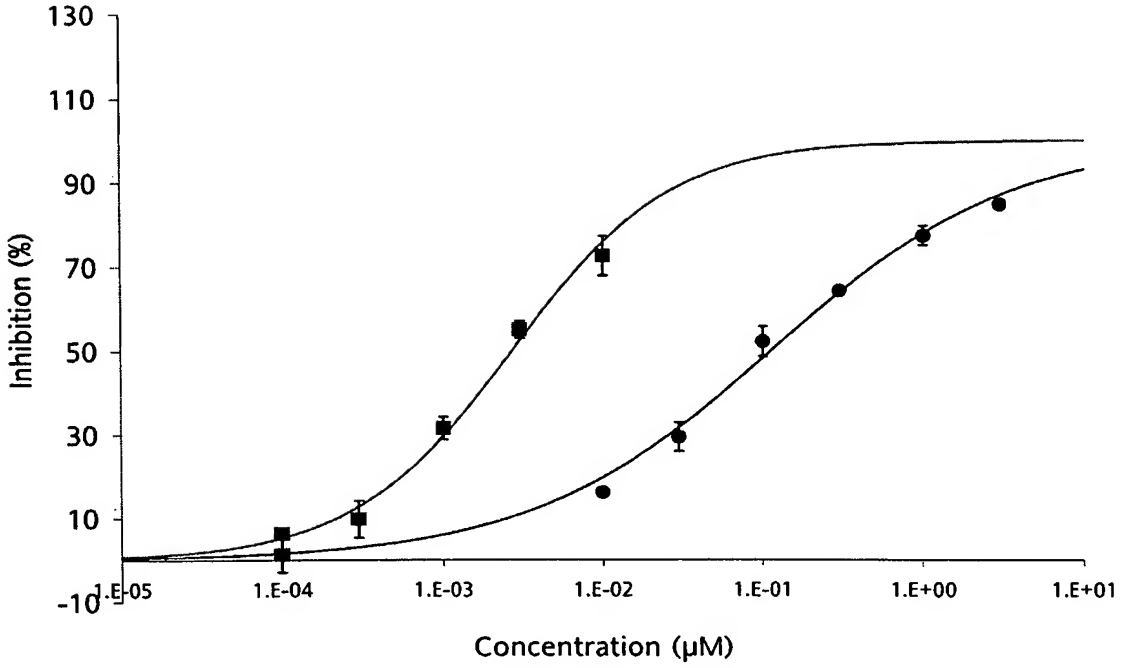

| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 1 (1036183) | 0.0286 μM | 0.94 |
| ■ Desipramine | 0.922 nM | 0.78 |

**Figure 48**



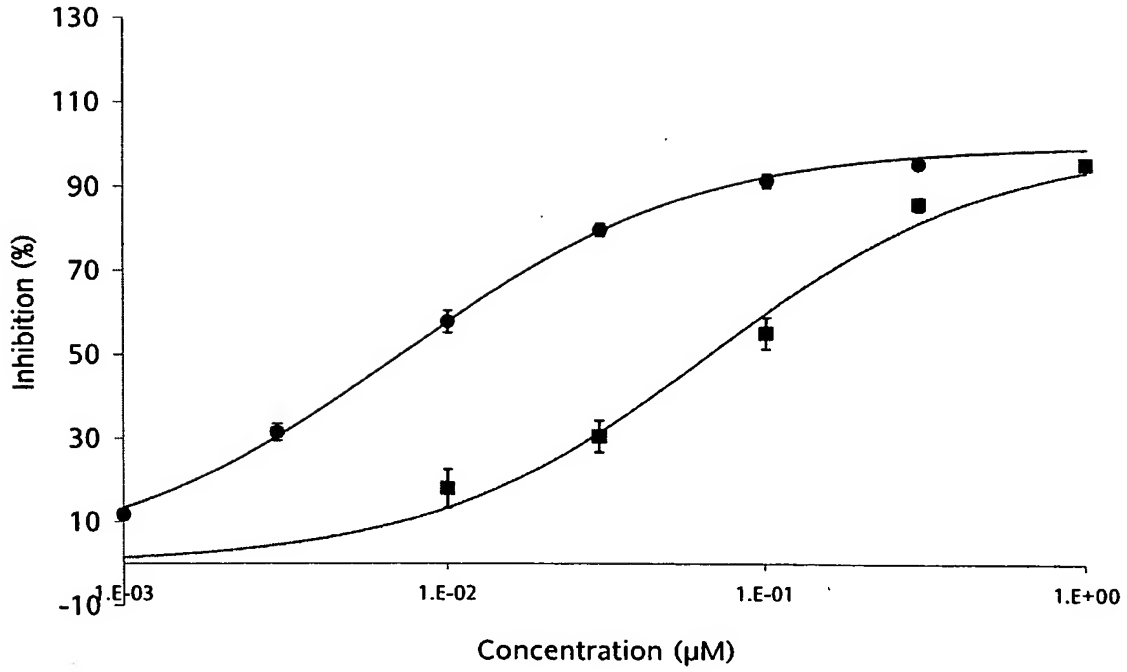

| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 1 (1036183) | 0.0217 μM | 0.766 |
| ■ Fluoxetine | 4.36 nM | 0.943 |

**Figure 49**



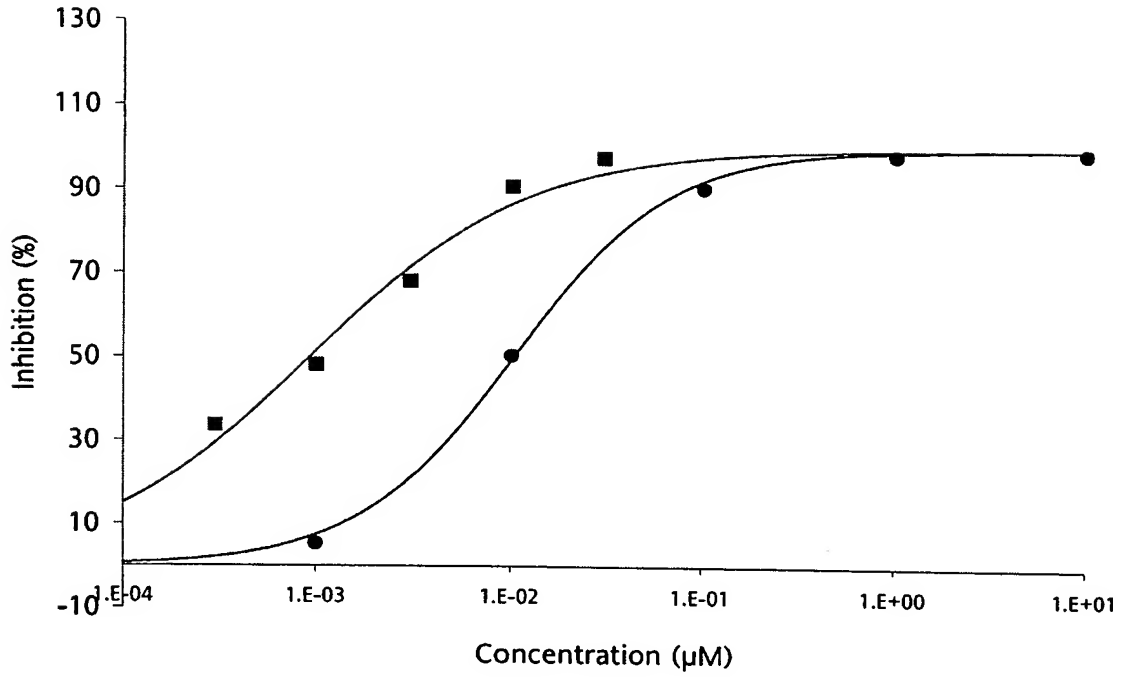

| Compound | $IC_{50}$ | $K_i$ | $n_H$ |
|---|---|---|---|
| CEL - 3 (1037044) | 0.112 ± 0.013 μM | 0.111 ± 0.013 μM | 0.584 ± 0.046 |
| ■ Desipramine | 2.78 ± 0.498 nM | 2.76 ± 0.494 nM | 0.872 ± 0.008 |

**Figure 50**



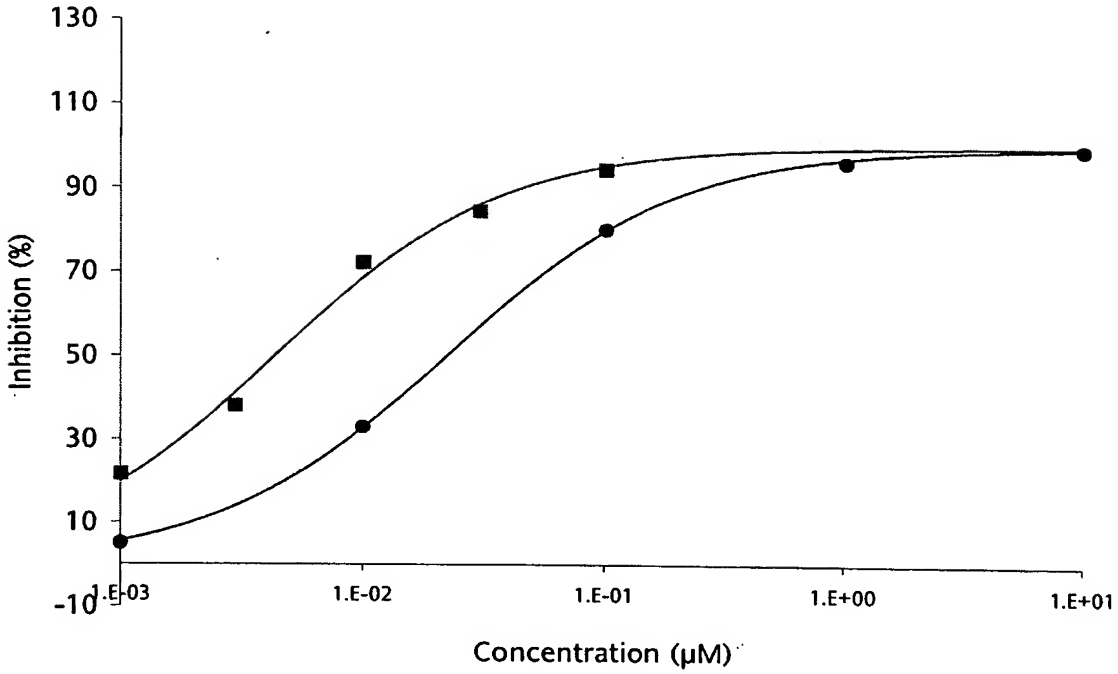

| Compound | $IC_{50}$ | $K_i$ | $n_H$ |
|---|---|---|---|
| ● CEL - 3 (1037044) | 7.3 ± 0.768 nM | 3.88 ± 0.408 nM | 0.949 ± 0.027 |
| ■ GBR-12909 | 0.0675 ± 0.0105 μM | 0.0359 ± 0.006 μM | 1.01 ± 0.105 |

**Figure 51**



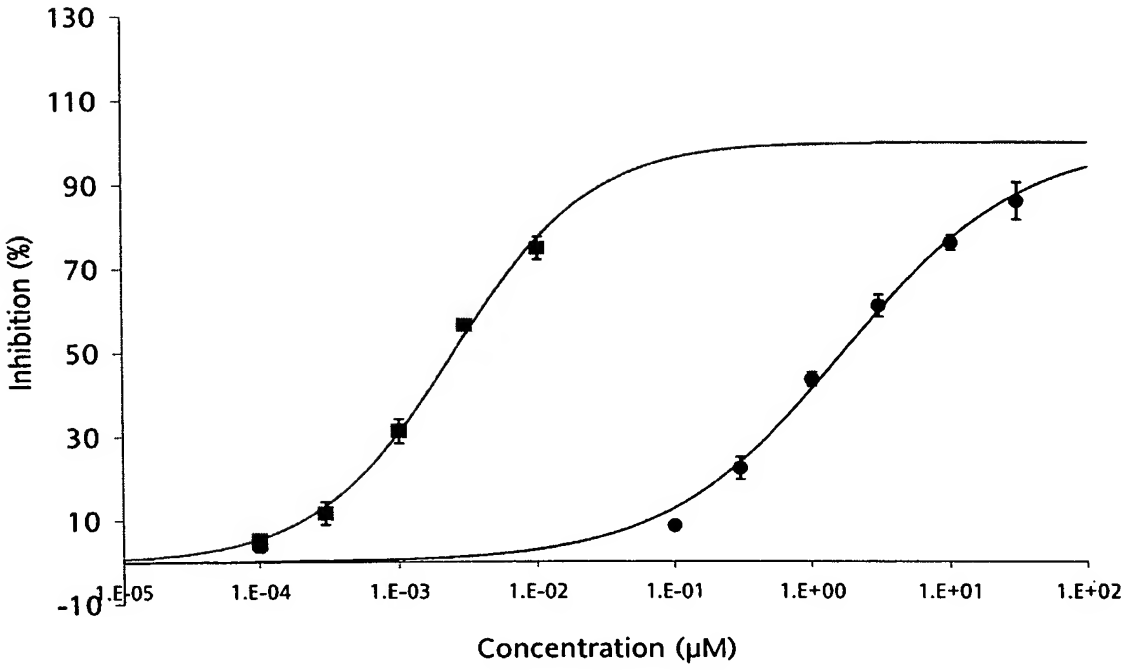

| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 3 (1037044) | 0.0103 μM | 1.08 |
| ■ Desipramine | 0.922 nM | 0.78 |

**Figure 52**



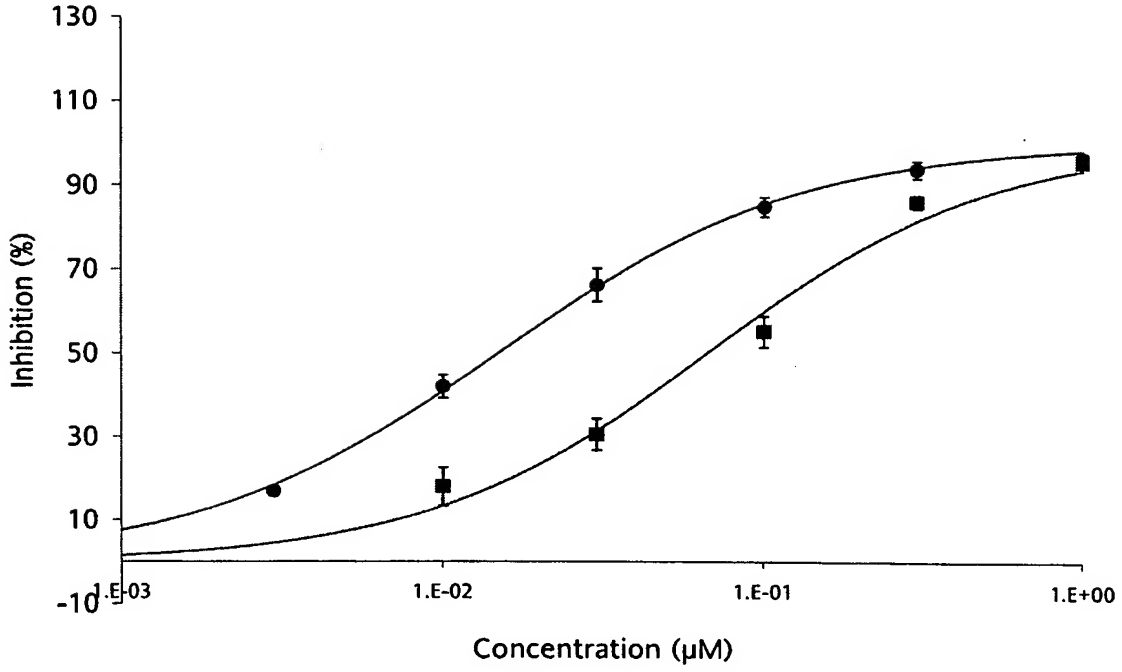

| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 3 (1037044) | 0.022 μM | 0.909 |
| ■ Fluoxetine | 4.36 nM | 0.943 |

**Figure 53**



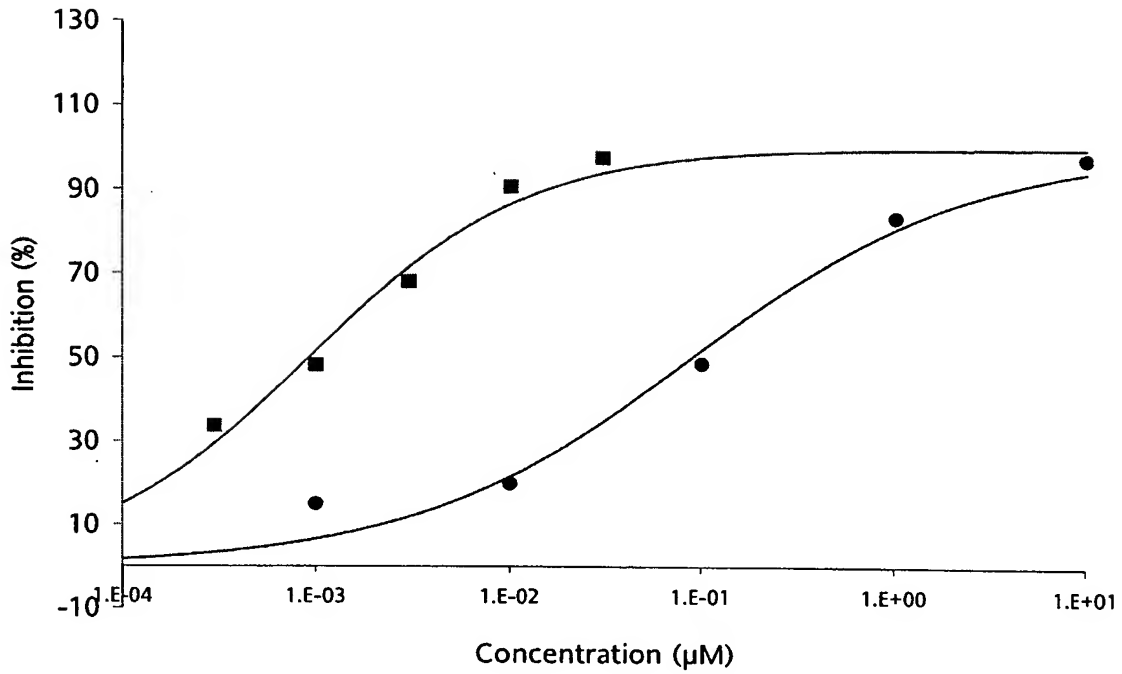

| Compound | $IC_{50}$ | $K_i$ | $n_H$ |
|---|---|---|---|
| CEL - 5 (1037045) | 1.68 ± 0.149 μM | 1.67 ± 0.148 μM | 0.679 ± 0.078 |
| ■ Desipramine | 2.52 ± 0.292 nM | 2.5 ± 0.289 nM | 0.882 ± 0.016 |

**Figure 54**



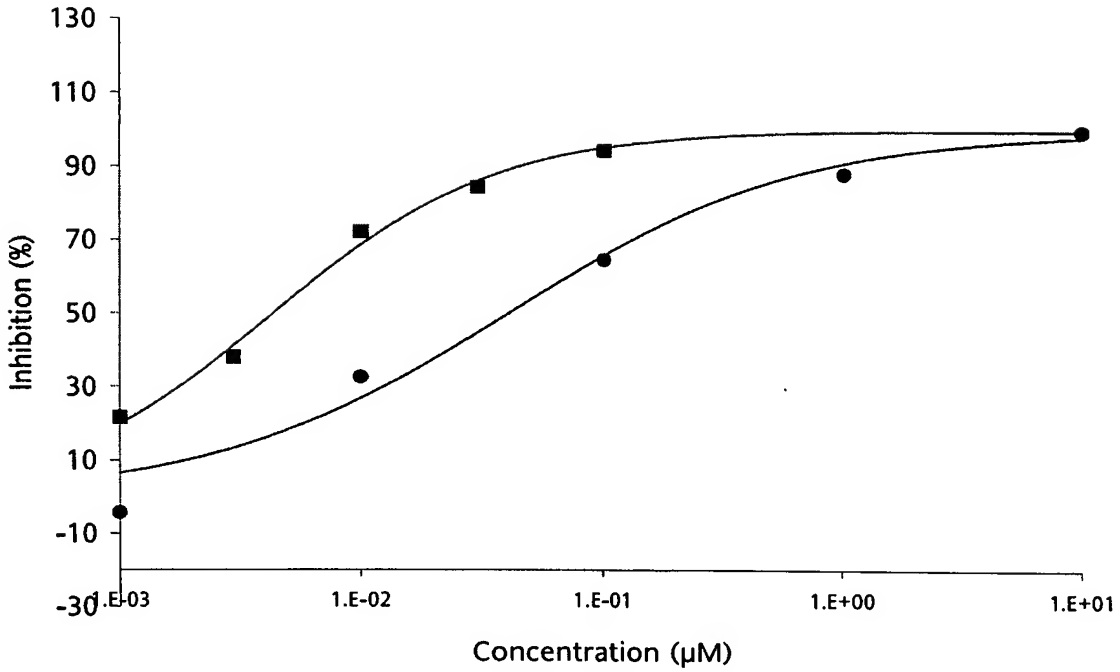

| Compound | $IC_{50}$ | $K_i$ | $n_H$ |
|---|---|---|---|
| CEL - 5 (1037045) | 0.0153 ± 0.002 μM | 8.15 ± 1.19 nM | 0.94 ± 0.054 |
| ■ GBR-12909 | 0.0675 ± 0.0105 μM | 0.0359 ± 0.006 μM | 1.01 ± 0.105 |

**Figure 55**




| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 5 (1037045) | 0.0885 μM | 0.592 |
| ■ Desipramine | 0.922 nM | 0.78 |

**Figure 56**




| Compound | $IC_{50}$ | $n_H$ |
|---|---|---|
| CEL - 5 (1037045) | 0.0403 μM | 0.718 |
| ■ Fluoxetine | 4.36 nM | 0.943 |

**Figure 57**

| CAT. # | ASSAY NAME | REFERENCE COMPOUND | HISTORICAL $IC_{50}/EC_{50}$ | CONCURRENT MIC BATCH * | CONCURRENT MIC $IC_{50}/EC_{50}$ |
|---|---|---|---|---|---|
| 302100 | Cytotoxicity, Norepinephrine Uptake - Antagonist | DMSO | 29 % | 95055 | 19.9 % |
| 364100 | Cytotoxicity, Serotonin Uptake - Antagonist | DMSO | 20 % | 95056 | 27.5 % |
| 302000 | Uptake, Norepinephrine | Desipramine | 1.9 nM | 94864 | 0.922 nM |
| 364000 | Uptake, Serotonin | Fluoxetine | 7.1 nM | 94865 | 4.36 nM |

* Batch: Represents compounds tested concurrently in the same assay(s).
‡ For some assays only a single concentration of reference compound is tested. Please refer to the individual response section (if applicable) of this report for the results.

## Figure 58

| CAT. # | ASSAY NAME | REFERENCE COMPOUND | HISTORICAL $IC_{50}$ | HISTORICAL $K_I$ | HISTORICAL $n_H$ | CONCURRENT MIC BATCH * | CONCURRENT MIC $IC_{50}$ |
|---|---|---|---|---|---|---|---|
| 118090 | CYP450, 3A4 | Ketoconazole | 0.22 µM | | | 95160 | 0.355 µM |
| 212610 | Bradykinin $B_2$ | Bradykinin | 0.89 nM | 0.53 nM | 0.9 | 94766 | 1.66 nM |
| 214510 | Calcium Channel L-Type, Benzothiazepine | Diltiazem | 0.036 µM | 0.032 µM | 0.9 | 94767 | 0.0873 µM |
| 204410 | Transporter, Norepinephrine (NET) | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 94760 | 0.767 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 94891 | 2.89 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 95109 | 1.94 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 95324 | 2.73 nM |
| | | Desipramine | 0.93 nM | 0.92 nM | 0.6 | 95371 | 3.67 nM |
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | GBR-12909 | 0.11 µM | 0.057 µM | 0.8 | 94762 | 0.0707 µM |
| | | GBR-12909 | 0.11 µM | 0.057 µM | 0.8 | 95110 | 0.0871 µM |
| | | GBR-12909 | 0.11 µM | 0.057 µM | 0.8 | 95326 | 0.0644 µM |
| | | GBR-12909 | 0.11 µM | 0.057 µM | 0.8 | 95372 | 0.0512 µM |

* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

**Figure 59**

## *PRIMARY TESTS*

| CAT. # | PRIMARY BIOCHEMICAL ASSAY | SPECIES | CONC. | % INH. | $IC_{50}$* | $K_i$ | $n_H$ |
|---|---|---|---|---|---|---|---|
| 204410 | Transporter, Norepinephrine (NET) | hum | 0.3 µM | 51 | 0.22 ± 0.01 µM | 0.218 ± 0.01 µM | 0.678 ± 0.042 |
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | hum | 0.03 µM | 63 | 0.0127 ± 0.001 µM | 6.73 ± 0.442 nM | 0.825 ± 0.0616 |

## *ABOVE PRIMARY TESTS IN RANK ORDER OF POTENCY*

| CAT. # | PRIMARY RADIOLIGAND ASSAY | SPECIES | CONC. | % INH. | $IC_{50}$* | $K_i$ | $n_H$ |
|---|---|---|---|---|---|---|---|
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | hum | 0.03 µM | 63 | 0.0127 ± 0.001 µM | 6.73 ± 0.442 nM | 0.825 ± 0.0616 |
| 204410 | Transporter, Norepinephrine (NET) | hum | 0.3 µM | 51 | 0.22 ± 0.01 µM | 0.218 ± 0.01 µM | 0.678 ± 0.042 |

*A standard error of the mean is presented where results are based on multiple, independent determinations.

gp=guinea pig; hum=human; syh=syrian hamster

**Figure 60**

| | PRIMARY TESTS | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PRIMARY BIOCHEMICAL ASSAY | | | | | | | |
| | COMPOUND | PT NUMBER | SPECIES | CONC. | % INH. | $IC_{50}$ * | $K_I$ | $n_H$ |
| 204410 | Transporter, Norepinephrine (NET) | | | | | | | |
| | Vial # 2 | 1037044 | hum | 0.1 µM | 51 | 0.112 ± 0.013 µM | 0.111 ± 0.0126 | 0.584 ± 0.046 |
| | Vial # 3 | 1037045 | hum | 3 µM | 57 | 1.68 ± 0.149 µM | 1.67 ± 0.148 µM | 0.679 ± 0.078 |
| 274020 | Transporter, Serotonin (5-Hydroxytryptamine) (SERT) | | | | | | | |
| | Vial # 2 | 1037044 | hum | 10 nM | 53 | 7.3 ± 0.768 nM | 3.88 ± 0.408 nM | 0.949 ± 0.0269 |
| | Vial # 3 | 1037045 | hum | 0.03 µM | 59 | 0.0153 ± 0.002 µM | 8.15 ± 1.19 nM | 0.94 ± 0.054 |

‡ Partially soluble in *in vitro* test solvent.
* A standard error of the mean is presented where results are based on multiple, independent determinations.
hum=human

**Figure 61**

| PRIMARY TESTS | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | PRIMARY CELLULAR ASSAY | | | | % RESPONSE | | |
| COMPOUND | PT NUMBER | SPECIES | CELL NAME | CONC. | CRITERIA | RESP. AG. | ANT. | $EC_{50}/IC_{50}$ * |
| 302000 Uptake, Norepinephrine | | | | | | | | |
| Vial #1 | 1036183 | hum | MDCK cells | 0.1 µM | ≥ ± 50% | | 78 | 0.0286 µM |
| Vial # 2 | 1037044 | hum | MDCK cells | 10 nM | ≥ ± 50% | | 50 | 0.0103 µM |
| Vial # 3 | 1037045 | hum | MDCK cells | 1 µM | ≥ ± 50% | | 83 | 0.0885 µM |
| 364000 Uptake, Serotonin (5-Hydroxytryptamine) | | | | | | | | |
| Vial #1 | 1036183 | hum | HEK-293 cells | 0.1 µM | ≥ ± 50% | | 75 | 0.0217 µM |
| Vial # 2 | 1037044 | hum | HEK-293 cells | 0.1 µM | ≥ ± 50% | | 80 | 0.022 µM |
| Vial # 3 | 1037045 | hum | HEK-293 cells | 0.1 µM | ≥ ± 50% | | 65 | 0.0403 µM |

‡ Partially soluble in *in vitro* test solvent.
* A standard error of the mean is presented where results are based on multiple, independent determinations.
Ag.=Agonist; Ant.=Antagonist; Resp.=Response; ND=Assay Test Not Done
hum=human

**Figure 62**

| COMPOUND | PT NUMBER | SECONDARY CELLULAR ASSAY SPECIES | CELL NAME | CONC. | CRITERIA | % RESPONSE RESP. | AG | ANT. | $EC_{50}/IC_{50}$ * |
|---|---|---|---|---|---|---|---|---|---|
| Prim. Cat#: 302000 | Sec. Cat#: 302100 | Cytotoxicity, Norepinephrine Uptake | | | | | | | |
| Vial #1 | 1036183 | hum | MDCK cells | 10 µM | ≥ ± 50% | | | | 9 |
| Vial # 2 | 1037044 | hum | MDCK cells | 10 µM | ≥ ± 50% | | | | 11 |
| Vial # 3 | 1037045 | hum | MDCK cells | 10 µM | ≥ ± 50% | | | | -6 |
| Prim. Cat#: 364000 | Sec. Cat#: 364100 | Cytotoxicity, Serotonin (5-Hydroxytryptamine) Uptake | | | | | | | |
| Vial #1 | 1036183 | hum | HEK-293 cells | 10 µM | ≥ ± 50% | | | | 2 |
| Vial # 2 | 1037044 | hum | HEK-293 cells | 10 µM | ≥ ± 50% | | | | -8 |
| Vial # 3 | 1037045 | hum | HEK-293 cells | 10 µM | ≥ ± 50% | | | | -3 |

‡ Partially soluble in *in vitro* test solvent.
* A standard error of the mean is presented where results are based on multiple, independent determinations.
♦ Denotes item meeting criteria for significance
Ag.=Agonist; Ant.=Antagonist; Resp.=Response; ND=Assay Test Not Done
hum=human

**Figure 63**

| Adverse Event | Frequency of Adverse Experiences (%) | | | |
|---|---|---|---|---|
| | Placebo N = 394 | 50 mg/day twice daily N = 426 | 100 mg/day twice daily N = 1871 | 200 mg/day twice daily N = 865 |
| Nausea | 10.9 | 12.7 | 11.2 | 19.4* |
| Headache | 17.0 | 14.6 | 8.0 | 13.5 |
| Increased Sweating | 1.3 | 14.0 | 4.3* | 11.6* |
| Constipation | 4.3 | 8.0 | 0.9 | 11.4* |
| Insomnia | 10.7 | 9.2 | 6.1 | 11.3 |
| Dry mouth | 5.6 | 8.0 | 7.9 | 9.0 |
| Vomiting | 3.6 | 3.8 | 3.0 | 7.9* |
| Abdominal Pain | 5.1 | 6.1 | 6.5 | 7.6 |
| Tremor | 1.5 | 0.9 | 2.5 | 6.7* |
| Anxiety | 1.3 | 2.3 | 4.1 | 5.1 |
| Palpitations | 1.8 | 2.3 | 2.7 | 4.6 |
| Vertigo | 1.8 | 3.0 | 5.0 | 4.5 |
| Fatigue | 3.0 | 2.8 | 2.5 | 4.4 |
| Dysuria | 0.3 | 1.4 | 2.1* | 3.7* |
| Hot flushes | 0 | 1.4 | 3.0 | 3.5 |
| Somnolence | 3.8 | 5.4 | 2.3 | 3.5 |
| Agitation | 3.0 | 1.6 | 3.0 | 2.9 |
| Nervousness | 2.0 | 4.2 | 2.3 | 2.8 |
| Dyspepsia | 4.1 | 3.5 | 2.1 | 2.2 |

* Significantly greater than placebo